ANTI-PHOSPHOCHOLINE ANTIBODIES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application Serial No. 63/452,798, filed March 17, 2023, the entire disclosure of which is hereby incorporated herein by reference.

REFERENCE TO SEQUENCE LISTING

[0002] This application contains a sequence listing which has been submitted electronically in ST.26 format and is hereby incorporated by reference in its entirety. Said ST.26 copy, created on March 15, 2024, is named "208485_seqlist.xml" and is 644,762 bytes in size.

FIELD

[0003] The present disclosure relates to antibodies that are specific for phosphocholine (PC), and methods of use thereof.

BACKGROUND

[0004] Phospholipids that contain polyunsaturated fatty acids are highly susceptible to modification by reactive oxygen species (ROS) and non-radical oxidizing agents. Oxidized lipids in cell membranes and in circulation can have both advantageous and harmful effects on the human body. Endogenous oxidized phospholipids (OxPL) have been shown to function as stress signals, causing phagocytes such as macrophages to respond by triggering inflammatory programs and eliminating the source of stress. However, excessive amounts of oxidized phospholipid products have been linked to chronic inflammation and the pathogenesis of various cardiopulmonary disorders, such as atherosclerosis and thrombosis, acute lung injury, and neurodegenerative processes.

[0005] Oxidized low-density lipoprotein (OxLDL) contains a number of OxPL species and is found in atherosclerotic lesions and detected at high concentration in sera from patients with hyperlipidemia, diabetes mellitus, and liver disease. The phosphocholine (PC) headgroup of OxPLs has been shown to be important for phospholipid binding to integral membrane proteins such as CD36 and the innate defense molecule C-reactive protein (CRP) (Boullier et al., *J Lipid Res*. 2005 May; 46(5): 969-76; Gershov et al., *J Exp Med*. 2000 Nov 6; 192(9): 1353-64).

[0006] Thus, there is a need for therapies, including antibodies, that bind PC for targeting OxPL across a wide range of diseases.

SUMMARY

[0007] The present disclosure provides polypeptides (*e.g.*, antibodies) that specifically bind to PC. Also provided are pharmaceutical compositions comprising these antibodies, nucleic acids encoding these antibodies, expression vectors and host cells for making these antibodies, and methods of treating a subject using these antibodies. The polypeptides provided herein are particularly advantageous because they bind PC with high affinity, display favorable stability, stress resistance, and immunogenicity profiles, and can be produced at high yields. The polypeptides provided herein are particularly useful for treating an inflammatory disorder or degenerative disease in a subject.

[0008] Accordingly, in one aspect, the present disclosure provides an antibody that specifically binds phosphocholine (PC), the antibody comprising: a VH comprising the CDRH1, CDRH2, and CDRH3 amino acid sequences of any one of the VH amino acid sequences set forth in SEQ ID NOs: 1-180; and a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences of any one of the VL amino acid sequences set forth in SEQ ID NOs: 181-368.

[0009] In an embodiment, the antibody comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences of the VH and VL amino acid sequences, respectively, set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and

267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368.

[0010] In an embodiment, the antibody comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383,

444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

[0011] In an embodiment, the antibody comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524,

591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588,

638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

[0012] In an embodiment, the antibody comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences, set forth in SEQ ID NOs: 369, 428, 484, 523, 591, and 656; 370, 429, 485, 523, 592, and 657; 371, 428, 486, 523, 593, and 658; 372, 428, 484, 523, 591, and 659; 373, 429, 484, 523, 594, and 659; 369, 428, 484, 523, 591, and 659; 374, 430, 484, 523, 591, and 659; 369, 428, 484, 523, 595, and 660; 375, 428, 487, 523, 596, and 659; 376, 428, 484, 524, 591, and 659; 377, 428, 484, 523, 591, and 661; 378, 428, 484, 523, 591, and 662; 372, 428, 484, 523, 597, and 658; 379, 428, 484, 523, 598, and 662; 372, 428, 488, 525, 599, and 659; 376, 431, 484, 523, 600, and 663; 380, 432, 484, 523, 591, and 664; 372, 428, 489, 523, 601, and 659; 381, 428, 490, 523, 591, and 659; 382, 428, 484, 526, 597, and 665; 381, 428, 491, 523, 602, and 659; 369, 428, 484, 527, 591, and 661; 377, 428, 492, 528, 591, and 662; 376, 433, 484, 529, 603, and 662; 383, 434, 484, 523, 604, and 666; 383, 428, 484, 523, 605, and 667; 384, 435, 484, 530, 606, and 659; 369, 436, 484, 523, 607, and 659; 372, 437, 487, 523, 591, and 659; 372, 428, 484, 523, 608, and 659; 385, 428, 493, 523, 609, and 662; 386, 428, 484, 531, 591, and 663; 372, 437, 484, 523, 608, and 661; 377, 428, 484, 523, 610, and 659; 387, 428, 484, 523, 611, and 668; 385, 428, 484, 523, 611, and 658; 372, 438, 484, 523, 596, and 662; 388, 428, 494, 523, 612, and 667; 369, 439, 484, 523, 613, and 668; 389, 428, 484, 523, 591, and 669; 382, 428, 484, 523, 591, and 663; 369, 428, 484, 523, 614, and 659; 381, 428, 484, 523, 591, and 659; 376, 440, 495, 523, 591, and 659; 381, 428, 484, 532, 615, and 662; 381, 428, 484, 523, 616, and 670; 390, 441, 484, 523, 591, and 659; 370, 442, 484, 523, 591, and 668; 391, 428, 484, 523, 617, and 671; 377, 428, 484, 533, 595, and 659; 377, 428, 484, 523, 618, and 659; 392, 432, 484, 523, 591, and 659; 377, 443, 484, 534, 619, and 662; 376, 428, 484, 535, 620, and 659; 393, 428, 484, 536, 621, and 659; 381, 428, 484, 537, 603, and 671; 383, 444, 489, 523, 622, and 59; 372, 428, 484, 523, 617, and 659; 377, 428, 484, 523, 623, and 659; 376, 428, 484, 538, 607, and 672; 369, 428, 484, 523, 616, and 671; 376, 428, 484, 523, 624, and 659; 394, 428, 484, 523, 591, and 659; 369, 428, 484, 523, 620, and 659; 383, 444, 496, 523, 625, and 660; 385, 428, 484, 523, 602, and 671; 376, 434, 484, 523, 591, and 659; 395, 445, 497, 523, 611, and 663; 396, 446, 487, 523, 626, and 670; 369, 428, 484, 523, 617, and 659; 392, 428, 484, 523, 591, and 662; 394, 428, 484, 523, 606, and 673; 393,

428, 498, 523, 591, and 659; 376, 428, 495, 523, 627, and 671; 369, 440, 484, 523, 628, and 671; 397, 428, 484, 539, 591, and 662; 389, 447, 484, 523, 591, and 659; 398, 448, 492, 523, 591, and 670; 373, 449, 490, 523, 611, and 659; 399, 428, 484, 537, 613, and 671; 400, 450, 484, 540, 598, and 659; 401, 428, 484, 541, 591, and 659; 390, 428, 484, 542, 629, and 659; 376, 428, 484, 523, 591, and 671; 400, 428, 499, 523, 591, and 659; 381, 428, 484, 523, 630, and 667; 384, 429, 484, 543, 631, and 659; 369, 428, 484, 523, 632, and 664; 402, 436, 484, 523, 597, and 661; 381, 451, 484, 523, 591, and 656; 403, 428, 484, 523, 633, and 659; 369, 429, 484, 544, 607, and 659; 404, 429, 484, 523, 630, and 659; 372, 429, 484, 523, 602, and 659; 381, 428, 484, 523, 591, and 665; 388, 428, 484, 523, 610, and 674; 405, 451, 484, 523, 634, and 671; 406, 428, 484, 545, 591, and 661; 400, 428, 484, 523, 635, and 667; 404, 428, 484, 546, 591, and 659; 384, 432, 500, 523, 636, and 664; 376, 452, 501, 547, 591, and 663; 407, 428, 484, 548, 619, and 659; 375, 428, 484, 523, 637, and 659; 372, 428, 484, 523, 607, and 659; 408, 428, 484, 523, 638, and 659; 386, 428, 484, 523, 591, and 659; 369, 428, 497, 523, 591, and 659; 403, 453, 484, 549, 591, and 659; 402, 454, 484, 523, 591, and 659; 383, 428, 484, 523, 591, and 659; 383, 434, 500, 523, 591, and 659; 376, 455, 502, 550, 591, and 675; 383, 435, 484, 523, 591, and 664; 369, 428, 484, 523, 602, and 659; 376, 428, 484, 551, 591, and 659; 376, 428, 484, 552, 591, and 659; 383, 428, 484, 553, 591, and 676; 376, 428, 484, 554, 591, and 659; 376, 428, 490, 523, 591, and 676; 369, 428, 503, 555, 606, and 659; 409, 428, 484, 523, 591, and 659; 383, 428, 504, 556, 591, and 659; 369, 434, 484, 523, 591, and 659; 390, 428, 484, 523, 637, and 677; 369, 456, 484, 523, 591, and 659; 370, 457, 484, 557, 591, and 659; 383, 428, 484, 558, 591, and 659; 404, 458, 499, 523, 591, and 659; 410, 428, 484, 523, 591, and 677; 383, 459, 484, 553, 639, and 659; 407, 428, 489, 549, 591, and 667; 374, 434, 484, 523, 591, and 659; 404, 428, 484, 559, 617, and 666; 411, 460, 505, 523, 591, and 672; 372, 429, 484, 523, 606, and 659; 383, 428, 485, 523, 591, and 659; 386, 460, 490, 523, 601, and 659; 412, 455, 493, 523, 592, and 670; 372, 428, 484, 560, 591, and 667; 372, 428, 484, 523, 606, and 659; 383, 461, 484, 523, 591, and 677; 369, 429, 484, 523, 606, and 659; 369, 434, 484, 530, 591, and 659; 376, 437, 484, 561, 603, and 666; 383, 462, 500, 523, 591, and 659; 383, 428, 484, 562, 591, and 659; 400, 463, 484, 523, 616, and 660; 376, 464, 484, 523, 602, and 677; 400, 434, 506, 549, 591, and 659; 369, 436, 507, 523, 591, and 659; 404, 429, 484, 523, 591, and 659; 384, 429, 484, 523, 616, and 659; 369, 429, 484, 523, 591, and 659; 377, 465, 484, 523, 630, and 660; 413, 459, 484, 563, 591, and 659; 369, 452, 484, 523, 591, and 663; 414, 466, 484, 523, 640, and 659; 373, 428, 484, 523, 591, and 659; 415, 428, 489, 564, 591, and 659; 369, 428, 484, 523, 591,

and 671; 400, 428, 484, 523, 641, and 677; 369, 428, 491, 565, 591, and 662; 403, 458, 508, 523, 642, and 664; 392, 467, 484, 523, 591, and 659; 369, 452, 509, 566, 643, and 659; 388, 468, 490, 523, 591, and 659; 369, 452, 484, 523, 644, and 667; 377, 440, 484, 567, 606, and 659; 370, 428, 484, 523, 591, and 656; 384, 467, 487, 523, 591, and 659; 392, 469, 510, 568, 591, and 659; 378, 464, 484, 523, 606, and 659; 377, 428, 484, 569, 645, and 659; 416, 434, 484, 523, 603, and 659; 370, 428, 484, 523, 606, and 659; 370, 428, 511, 570, 628, and 678; 369, 452, 484, 571, 630, and 663; 376, 428, 502, 572, 591, and 664; 417, 428, 484, 523, 591, and 665; 392, 428, 484, 573, 591, and 670; 376, 428, 512, 523, 646, and 659; 377, 428, 484, 574, 591, and 670; 383, 428, 484, 523, 647, and 667; 381, 428, 493, 575, 591, and 659; 383, 470, 501, 523, 591, and 659; 404, 471, 484, 537, 591, and 659; 418, 428, 484, 523, 635, and 670; 383, 472, 513, 576, 591, and 659; 419, 428, 484, 577, 606, and 659; 397, 428, 484, 523, 648, and 679; 372, 473, 484, 523, 591, and 664; 383, 474, 484, 523, 592, and 659; 372, 428, 484, 523, 591, and 663; 420, 434, 484, 523, 595, and 659; 370, 428, 514, 523, 591, and 659; 369, 428, 484, 523, 591, and 677; 383, 428, 484, 523, 600, and 659; 369, 475, 484, 523, 591, and 659; 421, 436, 484, 523, 649, and 664; 378, 452, 484, 523, 591, and 659; 376, 476, 515, 578, 641, and 659; 376, 428, 504, 523, 591, and 667; 422, 469, 484, 523, 606, and 660; 383, 461, 484, 523, 616, and 659; 369, 428, 484, 523, 650, and 656; 369, 428, 516, 523, 591, and 659; 405, 460, 484, 523, 618, and 659; 413, 431, 484, 523, 591, and 659; 382, 428, 484, 579, 621, and 671; 383, 428, 484, 523, 646, and 659; 372, 428, 484, 580, 591, and 660; 406, 429, 484, 527, 591, and 659; 383, 428, 517, 581, 595, and 659; 377, 437, 518, 582, 640, and 664; 369, 477, 487, 583, 651, and 659; 403, 464, 484, 534, 591, and 659; 383, 459, 484, 523, 606, and 659; 369, 454, 484, 584, 591, and 671; 372, 478, 519, 523, 591, and 680; 423, 429, 484, 523, 591, and 681; 383, 428, 484, 585, 591, and 659; 369, 434, 484, 557, 591, and 659; 382, 434, 484, 523, 649, and 659; 424, 479, 484, 523, 616, and 660; 376, 429, 484, 586, 591, and 666; 425, 428, 484, 523, 592, and 659; 369, 436, 484, 587, 652, and 659; 403, 428, 520, 588, 638, and 659; 417, 460, 484, 523, 591, and 659; 409, 460, 484, 523, 623, and 664; 404, 452, 484, 523, 591, and 659; 369, 428, 484, 523, 591, and 682; 383, 428, 521, 553, 653, and 659; 372, 480, 493, 523, 591, and 659; 369, 428, 484, 523, 654, and 659; 369, 477, 484, 523, 648, and 659; 369, 481, 484, 560, 591, and 659; 369, 452, 484, 523, 591, and 667; 409, 428, 484, 580, 606, and 659; 384, 452, 484, 589, 593, and 661; 377, 482, 484, 523, 591, and 659; 410, 483, 484, 523, 591, and 659; 384, 428, 489, 523, 591, and 659; 426, 429, 484, 523, 622, and 659; 376, 428, 484, 523, 637, and 676; 427, 428, 484, 523, 591, and 671; 373, 452, 506, 523, 591, and 659; 369, 428, 484, 590, 622, and 659; 369, 429,

521, 555, 591, and 661; 405, 428, 522, 523, 615, and 672; 376, 428, 510, 523, 591, and 659; 384, 428, 484, 523, 626, and 668; 410, 429, 484, 523, 591, and 659; 400, 452, 484, 523, 655, and 659; or 369, 434, 484, 523, 606, and 680.

[0013] In an embodiment, the antibody comprises the VH amino acid sequence of any one of SEQ ID NOs: 1-180.

[0014] In an embodiment, the antibody comprises the VL amino acid sequence of any one of SEQ ID NOs: 181-368.

[0015] In an embodiment, the VH and VL comprise the amino acid sequences, respectively, set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127

and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368.

[0016] In an embodiment, the antibody is a single-chain variable fragment (scFv).

[0017] In an embodiment, the antibody comprises a heavy chain constant region, or an Fc region thereof, optionally selected from the group consisting of a human IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2.

[0018] In an embodiment, the heavy chain constant region is a human IgG_1.

[0019] In an embodiment, the heavy chain constant region is a human IgG_4.

[0020] In an embodiment, the amino acid sequence of the human IgG_4 heavy chain constant region comprises a P at position 228, numbered according to the EU numbering system.

[0021] In an embodiment, the heavy chain constant region is a variant of a wild-type heavy chain constant region, wherein the variant heavy chain constant region binds to an Fc gamma receptor (FcγR) with lower affinity than the wild-type heavy chain constant region binds to the FcγR.

[0022] In an embodiment, the amino acid sequence of the heavy chain constant region comprises: A at position 234; A at position 235; A, Q or G at position 297; or A or G at position 329, in each case numbered according to the EU numbering system.

[0023] In an embodiment, the amino acid sequence of the heavy chain constant region comprises: A at positions 234 and 235; A at positions 234, 235, and 329; or A at positions 234, 235, and G at position 329, in each case numbered according to the EU numbering system.

[0024] In an embodiment, the heavy chain constant region is a variant of a wild-type heavy chain constant region, and wherein the variant heavy chain constant region has an increased

affinity for human neonatal Fc receptor (FcRn) at pH 6 relative to the affinity of the wild-type heavy chain constant region for human FcRn at pH 6.

[0025] In an embodiment, the amino acid sequence of the heavy chain constant region comprises: L and S at positions 428 and 434, respectively; K, F, and Y at positions 433, 434, and 436, respectively; or Y, T, and E at positions 252, 254, and 256, respectively, in each case numbered according to the EU numbering system.

[0026] In an embodiment, the antibody comprises a light chain constant region, optionally a human kappa or lambda constant region.

[0027] In one aspect, the present disclosure provides a polypeptide comprising a VH comprising the CDRH1, CDRH2, and CDRH3 amino acid sequences of any one of the VH amino acid sequences set forth in SEQ ID NOs: 1-180.

[0028] In an embodiment, the polypeptide comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and

499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

[0029] In an embodiment, the VH comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450,

and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

[0030] In an embodiment, the VH comprises any one of the amino acid sequences set forth in SEQ ID NOs: 1-180.

[0031] In one aspect, the present disclosure provides a polypeptide comprising a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences of any one of the VL amino acid sequences set forth in SEQ ID NOs: 181-368.

[0032] In an embodiment, the polypeptide comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523,

650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

[0033] In an embodiment, the VL comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602,

and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

[0034] In an embodiment, the VL comprises any one of the amino acid sequences set forth in SEQ ID NOs: 181-368.

[0035] In an embodiment, an antibody or polypeptide disclosed herein is conjugated to a cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.

[0036] In one aspect, the present disclosure provides a polynucleotide encoding a VH and/or a VL of an antibody disclosed herein, or a polypeptide disclosed herein.

[0037] In one aspect, the present disclosure provides a vector comprising the polynucleotide disclosed herein.

[0038] In an embodiment, the vector is an adeno-associated virus (AAV) vector.

[0039] In one aspect, the present disclosure provides a recombinant host cell comprising:

(a) a polynucleotide disclosed herein;

(b) a vector disclosed herein;

(c) a first polynucleotide encoding a VH or heavy chain of an antibody disclosed herein, and a second polynucleotide encoding a VL or light chain of an antibody disclosed herein; or

(d) a first vector comprising a first polynucleotide encoding a VH or heavy chain of an antibody disclosed herein, and a second vector comprising a second polynucleotide encoding a VL or light chain of an antibody disclosed herein.

[0040] In one aspect, the present disclosure provides a pharmaceutical composition comprising an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, or a host cell disclosed herein, and a pharmaceutically acceptable carrier or excipient.

[0041] In one aspect, the present disclosure provides a method of producing an antibody or polypeptide, the method comprising culturing a host cell disclosed herein under suitable conditions such that the polynucleotide is expressed, and the antibody or polypeptide is produced.

[0042] In one aspect, the present disclosure provides a method of inhibiting an activity of PC in a subject, the method comprising administering to the subject an effective amount of an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, a host cell disclosed herein, or a pharmaceutical composition disclosed herein.

[0043] In one aspect, the present disclosure provides a method of treating an inflammatory disorder or degenerative disease in a subject, the method comprising administering to the subject an effective amount of an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, a host cell disclosed herein, or a pharmaceutical composition disclosed herein.

[0044] In one aspect, the present disclosure provides use of an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, a host cell disclosed herein, or a pharmaceutical composition disclosed herein, for the manufacture of a medicament for the treatment of an inflammatory disorder or degenerative disease in a subject in need thereof.

[0045] In one aspect, the present disclosure provides an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, a host cell disclosed herein, or a pharmaceutical composition disclosed herein, for use in medicine.

[0046] In one aspect, the present disclosure provides an antibody or polypeptide disclosed herein, a polynucleotide disclosed herein, a vector disclosed herein, a host cell disclosed herein, or a pharmaceutical composition disclosed herein, for use in the treatment of an inflammatory disorder or degenerative disease in a subject in need thereof.

[0047] In an embodiment, the inflammatory disorder or degenerative disease is selected from the group consisting of organ reperfusion injury such as myocardial infarction induced reperfusion injury, Kawasaki disease, non-alcoholic steatohepatitis (NASH), organ transplant rejection, atherosclerosis, Type I or Type 2 Diabetes, rheumatoid arthritis, osteoporosis, acute lung injury, asthma, chronic obstructive pulmonary disease (COPD), lung fibrosis, pain, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), age-related macular degeneration (AMD), stroke, Huntington's disease, frontotemporal dementia (FTD), multiple sclerosis (MS), isolated demyelinating diseases of the central nervous system, osteoarthritis, Crohn's Disease, and ulcerative colitis.

DETAILED DESCRIPTION

[0048] The instant disclosure provides polypeptides (*e.g.*, antibodies) that specifically bind to PC. Also provided are pharmaceutical compositions comprising these polypeptides, nucleic acids encoding these polypeptides, expression vectors and host cells for making these polypeptides, and methods of treating a subject using these polypeptides. The polypeptides provided herein are particularly advantageous because they bind PC with high affinity, display favorable stability, stress resistance, and immunogenicity profiles, and can be produced at high yields. The polypeptides provided herein are particularly useful for treating an inflammatory disorder or degenerative disease in a subject.

Definitions

[0049] As used herein, the terms "antibody" and "antibodies" include full-length antibodies, antigen-binding fragments of full-length antibodies, and molecules comprising antibody CDRs, VH regions, and/or VL regions. Examples of antibodies include, without limitation, monoclonal antibodies, recombinantly produced antibodies, monospecific antibodies, multispecific antibodies (including bispecific antibodies), human antibodies, humanized antibodies, chimeric antibodies, immunoglobulins, synthetic antibodies, tetrameric antibodies comprising two heavy chain and two light chain molecules, an antibody light chain monomer, an antibody heavy chain monomer, an antibody light chain dimer, an antibody heavy chain dimer, an antibody light chain-antibody heavy chain pair, intrabodies, heteroconjugate antibodies, antibody-drug conjugates, single domain antibodies, monovalent antibodies, single-chain antibodies or single-chain Fvs (scFv), camelized antibodies, affibodies, Fab fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), anti-

idiotypic (anti-Id) antibodies (including, *e.g.*, anti-anti-Id antibodies), and antigen-binding fragments of any of the above. In certain embodiments, antibodies described herein refer to polyclonal antibody populations. Antibodies can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA, or IgY), any class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, or IgA_2), or any subclass (*e.g.*, IgG_2a or IgG_2b) of immunoglobulin molecule. In certain embodiments, antibodies described herein are IgG antibodies, or a class (*e.g.*, human IgG_1 or IgG_4) or subclass thereof. In a specific embodiment, the antibody is a humanized monoclonal antibody. In another specific embodiment, the antibody is a human monoclonal antibody.

[0050] "Multispecific antibodies" are antibodies (*e.g.*, bispecific antibodies) that specifically bind to two or more different antigens or two or more different regions of the same antigen. Multispecific antibodies include bispecific antibodies that contain two different antigen-binding sites (exclusive of the Fc region). Multispecific antibodies can include, for example, recombinantly produced antibodies, human antibodies, humanized antibodies, resurfaced antibodies, chimeric antibodies, immunoglobulins, synthetic antibodies, tetrameric antibodies comprising two heavy chain and two light chain molecules, an antibody light chain monomer, heteroconjugate antibodies, linked single-chain antibodies or linked-single-chain Fvs (scFv), camelized antibodies, affybodies, linked Fab fragments, $F(ab')_2$ fragments, chemically-linked Fvs, and disulfide-linked Fvs (sdFv). Multispecific antibodies can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA, or IgY), any class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, or IgA_2), or any subclass (*e.g.*, IgG_2a or IgG_2b) of immunoglobulin molecule. In certain embodiments, multispecific antibodies described herein are IgG antibodies, or a class (*e.g.*, human IgG_1, IgG_2, or IgG_4) or subclass thereof.

[0051] As used herein, the term "CDR" or "complementarity determining region" means the noncontiguous antigen combining sites found within the variable regions of heavy and light chain polypeptides. These particular regions have been described by, for example, Kabat *et al.*, J. Biol. Chem. 252, 6609-6616 (1977) and Kabat *et al.*, Sequences of protein of immunological interest. (1991), by Chothia *et al.*, J. Mol. Biol. 196:901-917 (1987), and by MacCallum *et al.*, J. Mol. Biol. 262:732-745 (1996), all of which are herein incorporated by reference in their entireties, where the definitions include overlapping or subsets of amino acid residues when compared against each other. In certain embodiments, the term "CDR" is a CDR as defined by MacCallum *et al.*, J. Mol. Biol. 262:732-745 (1996) and Martin A. "Protein Sequence and Structure Analysis of Antibody Variable Domains," in *Antibody Engineering*, Kontermann and Dübel, eds., Chapter 31, pp. 422-

439, Springer-Verlag, Berlin (2001). In certain embodiments, the term "CDR" is a CDR as defined by Kabat *et al.,* J. Biol. Chem. 252, 6609-6616 (1977) and Kabat *et al.,* Sequences of protein of immunological interest. (1991). In certain embodiments, heavy chain CDRs and light chain CDRs of an antibody are defined using different conventions. In certain embodiments, heavy chain CDRs and/or light chain CDRs are defined by performing structural analysis of an antibody and identifying residues in the variable region(s) predicted to make contact with an epitope region of a target molecule (*e.g.*, PC). CDRH1, CDRH2, and CDRH3 denote the heavy chain CDRs, and CDRL1, CDRL2, and CDRL3 denote the light chain CDRs.

[0052] As used herein, the terms "variable region" and "variable domain" are used interchangeably and are common in the art. The variable region typically refers to a portion of an antibody, generally, a portion of a light or heavy chain, typically about the amino-terminal 110 to 120 amino acids or 110 to 125 amino acids in the mature heavy chain and about 90 to 115 amino acids in the mature light chain, which differ extensively in sequence among antibodies and are used in the binding and specificity of a particular antibody for its particular antigen. The variability in sequence is concentrated in those regions called complementarity determining regions (CDRs) while the more highly conserved regions in the variable region are called framework regions (FR). Without wishing to be bound by any particular mechanism or theory, it is believed that the CDRs of the light and heavy chains are primarily responsible for the interaction and specificity of the antibody with antigen. In certain embodiments, the variable region is a human variable region. In certain embodiments, the variable region comprises rodent or murine CDRs and human framework regions (FRs). In certain embodiments, the variable region comprises rodent or murine CDRs and primate (*e.g.*, non-human primate) framework regions (FRs).

[0053] As used herein, the terms "VH" and "VL" refer to antibody heavy and light chain variable regions, respectively, as described in Kabat *et al.*, (1991) Sequences of Proteins of Immunological Interest (NIH Publication No. 91-3242, Bethesda), which is herein incorporated by reference in its entirety.

[0054] As used herein, the term "constant region" is common in the art. The constant region is an antibody portion, *e.g.*, a carboxyl terminal portion of a light and/or heavy chain, which is not directly involved in binding of an antibody to antigen but which can exhibit various effector functions, such as interaction with an Fc receptor (*e.g.*, Fc gamma receptor).

[0055] As used herein, the term "heavy chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, alpha (α), delta (δ), epsilon (ε), gamma (γ), and mu (μ), based on the amino acid sequence of the constant region, which give rise to IgA, IgD, IgE, IgG, and IgM classes of antibodies, respectively, including subclasses of IgG, *e.g.*, IgG_1, IgG_2, IgG_3, and IgG_4.

[0056] As used herein, the term "light chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, kappa (κ) or lambda (λ), based on the amino acid sequence of the constant region. Light chain amino acid sequences are well known in the art. In specific embodiments, the light chain is a human light chain.

[0057] As used herein, the terms "specifically binds," "specifically recognizes," "immunospecifically binds," and "immunospecifically recognizes" are analogous terms in the context of antibodies and refer to molecules that bind to an antigen (*e.g.*, epitope or immune complex) as such binding is understood by one skilled in the art. For example, a molecule that specifically binds to an antigen can bind to other peptides or polypeptides, generally with lower affinity as determined by, *e.g.*, immunoassays, BIAcore®, KinExA 3000 instrument (Sapidyne Instruments, Boise, ID), or other assays known in the art. In a specific embodiment, molecules that specifically bind to an antigen bind to the antigen with a K_A that is at least 2 logs (*e.g.*, factors of 10), 2.5 logs, 3 logs, 4 logs, or greater than the K_A when the molecules bind non-specifically to another antigen.

[0058] As used herein, the term "affinity" refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (*e.g.*, an antibody) and its binding partner (*e.g.*, an antigen). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (*e.g.*, antibody and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (Kd). Affinity can be measured by common methods known in the art, including those described herein.

[0059] As used herein, the term "EU numbering system" refers to the EU numbering convention for the constant regions of an antibody, as described in Edelman, G.M. *et al.*, Proc. Natl. Acad. USA, 63, 78-85 (1969) and Kabat *et al*, Sequences of Proteins of Immunological Interest, U.S. Dept. Health and Human Services, 5th edition, 1991, each of which is herein incorporated by reference in its entirety.

[0060] As used herein, the term "treat," "treating," and "treatment" refer to therapeutic or preventative measures described herein. The methods of "treatment" employ administration of an antibody to a subject having a disease or disorder, or predisposed to having such a disease or disorder, in order to prevent, cure, delay, reduce the severity of, or ameliorate one or more symptoms of the disease or disorder or recurring disease or disorder, or in order to prolong the survival of a subject beyond that expected in the absence of such treatment.

[0061] As used herein, the term "effective amount" in the context of the administration of a therapy to a subject refers to the amount of a therapy that achieves a desired prophylactic or therapeutic effect.

[0062] As used herein, the term "subject" includes any human or non-human animal. In certain embodiments, the subject is a human or non-human mammal. In certain embodiments, the subject is a human.

[0063] As used herein with respect to an antibody or polynucleotide, the term "isolated" refers to an antibody or polynucleotide that is separated from one or more contaminants (*e.g.*, polypeptides, polynucleotides, lipids, or carbohydrates, etc.) which are present in a natural source of the antibody or polynucleotide. All instances of "isolated antibodies" described herein are additionally contemplated as antibodies that may be, but need not be, isolated. All instances of "isolated polynucleotides" described herein are additionally contemplated as polynucleotides that may be, but need not be, isolated. All instances of "antibodies" described herein are additionally contemplated as antibodies that may be, but need not be, isolated. All instances of "polynucleotides" described herein are additionally contemplated as polynucleotides that may be, but need not be, isolated.

[0064] The determination of "percent identity" between two sequences (*e.g.*, amino acid sequences or nucleic acid sequences) can be accomplished using a mathematical algorithm. A specific, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin S & Altschul SF (1990) PNAS 87: 2264-2268, modified as in Karlin S & Altschul SF (1993) PNAS 90: 5873-5877, each of which is herein incorporated by reference in its entirety. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul SF *et al.*, (1990) J Mol Biol 215: 403, which is herein incorporated by reference in its entirety. BLAST nucleotide searches can be performed with the NBLAST nucleotide program parameters set, *e.g.*, for score=100, wordlength=12 to obtain nucleotide

sequences homologous to a nucleic acid molecule described herein. BLAST protein searches can be performed with the XBLAST program parameters set, *e.g.*, to score 50, wordlength=3 to obtain amino acid sequences homologous to a protein molecule described herein. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul SF *et al.*, (1997) Nuc Acids Res 25: 3389-3402, which is herein incorporated by reference in its entirety. Alternatively, PSI BLAST can be used to perform an iterated search which detects distant relationships between molecules (*Id.*). When utilizing BLAST, Gapped BLAST, and PSI Blast programs, the default parameters of the respective programs (*e.g.*, of XBLAST and NBLAST) can be used (*see, e.g.*, National Center for Biotechnology Information (NCBI) on the worldwide web, ncbi.nlm.nih.gov). Another specific, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, 1988, CABIOS 4:11-17, which is herein incorporated by reference in its entirety. Such an algorithm is incorporated in the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

[0065] The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted.

Anti-PC Antibodies

[0066] In one aspect, the instant disclosure provides polypeptides (*e.g.*, antibodies) that specifically bind to PC. The amino acid sequences of exemplary antibodies are set forth in Table 1.

Table 1: Amino Acid Sequences of Exemplary Antibodies.

	SEQ ID NO:							
Antibody	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB01_A06	1	181	369	428	484	523	591	656
PcOxP_DB01_A12	2	182	370	429	485	523	592	657
PcOxP_DB01_B01	3	183	371	428	486	523	593	658
PcOxP_DB01_B04	4	184	372	428	484	523	591	659
PcOxP_DB01_B05	5	185	373	429	484	523	594	659
PcOxP_DB01_B07	1	184	369	428	484	523	591	659
PcOxP_DB01_B08	6	184	374	430	484	523	591	659

Antibody	SEQ ID NO:							
	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB01_B09	1	186	369	428	484	523	595	660
PcOxP_DB01_B11	7	187	375	428	487	523	596	659
PcOxP_DB01_C01	8	188	376	428	484	524	591	659
PcOxP_DB01_C03	9	189	377	428	484	523	591	661
PcOxP_DB01_C04	10	190	378	428	484	523	591	662
PcOxP_DB01_C05	4	191	372	428	484	523	597	658
PcOxP_DB01_C06	11	192	379	428	484	523	598	662
PcOxP_DB01_C08	12	193	372	428	488	525	599	659
PcOxP_DB01_C12	13	194	376	431	484	523	600	663
PcOxP_DB01_D02	14	195	380	432	484	523	591	664
PcOxP_DB01_D05	15	196	372	428	489	523	601	659
PcOxP_DB01_D08	16	184	381	428	490	523	591	659
PcOxP_DB01_D09	17	197	382	428	484	526	597	665
PcOxP_DB01_E04	18	198	381	428	491	523	602	659
PcOxP_DB01_E05	1	199	369	428	484	527	591	661
PcOxP_DB01_E06	19	200	377	428	492	528	591	662
PcOxP_DB01_E11	20	201	376	433	484	529	603	662
PcOxP_DB01_F04	21	202	383	434	484	523	604	666
PcOxP_DB01_F10	22	203	383	428	484	523	605	667
PcOxP_DB01_G01	23	204	384	435	484	530	606	659
PcOxP_DB01_G09	24	205	369	436	484	523	607	659
PcOxP_DB01_G11	25	184	372	437	487	523	591	659
PcOxP_DB01_G12	4	206	372	428	484	523	608	659
PcOxP_DB01_H04	26	207	385	428	493	523	609	662
PcOxP_DB01_H08	27	208	386	428	484	531	591	663
PcOxP_DB01_H10	28	209	372	437	484	523	608	661
PcOxP_DB02_A06	9	210	377	428	484	523	610	659
PcOxP_DB02_A09	29	211	387	428	484	523	611	668
PcOxP_DB02_A10	30	212	385	428	484	523	611	658
PcOxP_DB02_A11	31	213	372	438	484	523	596	662
PcOxP_DB02_A12	32	214	388	428	494	523	612	667
PcOxP_DB02_B02	33	215	369	439	484	523	613	668
PcOxP_DB02_B06	34	216	389	428	484	523	591	669
PcOxP_DB02_B10	17	217	382	428	484	523	591	663
PcOxP_DB02_B12	1	218	369	428	484	523	614	659
PcOxP_DB02_C01	35	184	381	428	484	523	591	659
PcOxP_DB02_C02	36	184	376	440	495	523	591	659
PcOxP_DB02_C06	35	219	381	428	484	532	615	662
PcOxP_DB02_C09	35	220	381	428	484	523	616	670
PcOxP_DB02_C11	37	184	390	441	484	523	591	659
PcOxP_DB02_D01	38	221	370	442	484	523	591	668
PcOxP_DB02_D09	39	222	391	428	484	523	617	671
PcOxP_DB02_D10	9	223	377	428	484	533	595	659

Antibody	SEQ ID NO:							
	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB02_E01	9	224	377	428	484	523	618	659
PcOxP_DB02_E06	40	184	392	432	484	523	591	659
PcOxP_DB02_E10	41	225	377	443	484	534	619	662
PcOxP_DB02_F02	8	226	376	428	484	535	620	659
PcOxP_DB02_F07	42	227	393	428	484	536	621	659
PcOxP_DB02_F12	35	228	381	428	484	537	603	671
PcOxP_DB02_G06	43	229	383	444	489	523	622	659
PcOxP_DB02_G07	4	230	372	428	484	523	617	659
PcOxP_DB02_G09	9	231	377	428	484	523	623	659
PcOxP_DB02_H03	8	232	376	428	484	538	607	672
PcOxP_DB02_H10	1	233	369	428	484	523	616	671
PcOxP_DB03_A03	8	234	376	428	484	523	624	659
PcOxP_DB03_A08	44	184	394	428	484	523	591	659
PcOxP_DB03_A09	1	235	369	428	484	523	620	659
PcOxP_DB03_A11	45	236	383	444	496	523	625	660
PcOxP_DB03_B02	30	237	385	428	484	523	602	671
PcOxP_DB03_C03	46	184	376	434	484	523	591	659
PcOxP_DB03_C06	47	238	395	445	497	523	611	663
PcOxP_DB03_C11	48	239	396	446	487	523	626	670
PcOxP_DB03_C12	1	230	369	428	484	523	617	659
PcOxP_DB03_D01	49	190	392	428	484	523	591	662
PcOxP_DB03_D07	44	240	394	428	484	523	606	673
PcOxP_DB03_D08	50	184	393	428	498	523	591	659
PcOxP_DB03_D11	51	241	376	428	495	523	627	671
PcOxP_DB03_E01	52	242	369	440	484	523	628	671
PcOxP_DB03_E02	53	243	397	428	484	539	591	662
PcOxP_DB03_E07	54	184	389	447	484	523	591	659
PcOxP_DB03_E08	55	244	398	448	492	523	591	670
PcOxP_DB03_E09	56	245	373	449	490	523	611	659
PcOxP_DB03_F01	57	246	399	428	484	537	613	671
PcOxP_DB03_F10	58	247	400	450	484	540	598	659
PcOxP_DB03_G02	59	248	401	428	484	541	591	659
PcOxP_DB03_G03	60	249	390	428	484	542	629	659
PcOxP_DB03_G06	8	250	376	428	484	523	591	671
PcOxP_DB03_G07	61	184	400	428	499	523	591	659
PcOxP_DB03_G10	35	251	381	428	484	523	630	667
PcOxP_DB03_H03	62	252	384	429	484	543	631	659
PcOxP_DB03_H07	1	253	369	428	484	523	632	664
PcOxP_DB03_H08	63	254	402	436	484	523	597	661
PcOxP_DB03_H09	64	181	381	451	484	523	591	656
PcOxP_DB04_A07	65	255	403	428	484	523	633	659
PcOxP_DB04_A09	66	256	369	429	484	544	607	659
PcOxP_DB04_A10	67	257	404	429	484	523	630	659

Antibody	SEQ ID NO:							
	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB04_A12	68	198	372	429	484	523	602	659
PcOxP_DB04_B06	35	258	381	428	484	523	591	665
PcOxP_DB04_B08	69	259	388	428	484	523	610	674
PcOxP_DB04_C03	70	260	405	451	484	523	634	671
PcOxP_DB04_C08	71	261	406	428	484	545	591	661
PcOxP_DB04_D08	72	262	400	428	484	523	635	667
PcOxP_DB04_F06	73	263	404	428	484	546	591	659
PcOxP_DB04_F11	74	264	384	432	500	523	636	664
PcOxP_DB04_G06	75	265	376	452	501	547	591	663
PcOxP_DB04_H03	76	266	407	428	484	548	619	659
PcOxP_DB04_H07	77	267	375	428	484	523	637	659
PcOxP_DB04_H08	4	205	372	428	484	523	607	659
PcOxP_DB04_H10	78	268	408	428	484	523	638	659
PcOxP_DB01_A03	1	269	369	428	484	523	591	659
PcOxP_DB01_A04	27	269	386	428	484	523	591	659
PcOxP_DB01_A05	79	269	369	428	497	523	591	659
PcOxP_DB01_A08	80	270	403	453	484	549	591	659
PcOxP_DB01_B02	81	269	402	454	484	523	591	659
PcOxP_DB01_B03	22	269	383	428	484	523	591	659
PcOxP_DB01_B06	82	269	383	434	500	523	591	659
PcOxP_DB01_B10	83	271	376	455	502	550	591	675
PcOxP_DB01_B12	84	272	383	435	484	523	591	664
PcOxP_DB01_C07	1	273	369	428	484	523	602	659
PcOxP_DB01_C09	8	274	376	428	484	551	591	659
PcOxP_DB01_C10	8	275	376	428	484	552	591	659
PcOxP_DB01_D01	22	276	383	428	484	553	591	676
PcOxP_DB01_D04	8	277	376	428	484	554	591	659
PcOxP_DB01_D06	85	278	376	428	490	523	591	676
PcOxP_DB01_D07	86	279	369	428	503	555	606	659
PcOxP_DB01_D10	87	269	409	428	484	523	591	659
PcOxP_DB01_D11	88	280	383	428	504	556	591	659
PcOxP_DB01_D12	89	269	369	434	484	523	591	659
PcOxP_DB01_E01	60	281	390	428	484	523	637	677
PcOxP_DB01_E02	90	269	369	456	484	523	591	659
PcOxP_DB01_E03	91	282	370	457	484	557	591	659
PcOxP_DB01_E07	22	283	383	428	484	558	591	659
PcOxP_DB01_E08	92	269	404	458	499	523	591	659
PcOxP_DB01_E09	93	284	410	428	484	523	591	677
PcOxP_DB01_E10	94	285	383	459	484	553	639	659
PcOxP_DB01_F01	95	286	407	428	489	549	591	667
PcOxP_DB01_F03	96	269	374	434	484	523	591	659
PcOxP_DB01_F06	73	287	404	428	484	559	617	666
PcOxP_DB01_F07	97	288	411	460	505	523	591	672

Antibody	SEQ ID NO:							
	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB01_F08	68	289	372	429	484	523	606	659
PcOxP_DB01_F11	98	269	383	428	485	523	591	659
PcOxP_DB01_F12	99	290	386	460	490	523	601	659
PcOxP_DB01_G02	100	291	412	455	493	523	592	670
PcOxP_DB01_G03	4	292	372	428	484	560	591	667
PcOxP_DB01_G04	4	289	372	428	484	523	606	659
PcOxP_DB01_G05	101	284	383	461	484	523	591	677
PcOxP_DB01_G06	66	289	369	429	484	523	606	659
PcOxP_DB01_G07	89	293	369	434	484	530	591	659
PcOxP_DB01_G10	102	294	376	437	484	561	603	666
PcOxP_DB01_H01	103	269	383	462	500	523	591	659
PcOxP_DB01_H02	22	295	383	428	484	562	591	659
PcOxP_DB01_H03	104	296	400	463	484	523	616	660
PcOxP_DB01_H06	105	297	376	464	484	523	602	677
PcOxP_DB01_H07	106	270	400	434	506	549	591	659
PcOxP_DB01_H09	107	269	369	436	507	523	591	659
PcOxP_DB02_A04	67	269	404	429	484	523	591	659
PcOxP_DB02_A05	62	298	384	429	484	523	616	659
PcOxP_DB02_B04	66	269	369	429	484	523	591	659
PcOxP_DB02_B07	108	299	377	465	484	523	630	660
PcOxP_DB02_B09	109	300	413	459	484	563	591	659
PcOxP_DB02_C03	110	301	369	452	484	523	591	663
PcOxP_DB02_C04	111	302	414	466	484	523	640	659
PcOxP_DB02_C05	112	269	373	428	484	523	591	659
PcOxP_DB02_C08	113	303	415	428	489	564	591	659
PcOxP_DB02_C10	1	304	369	428	484	523	591	671
PcOxP_DB02_C12	72	305	400	428	484	523	641	677
PcOxP_DB02_D02	114	306	369	428	491	565	591	662
PcOxP_DB02_D03	115	307	403	458	508	523	642	664
PcOxP_DB02_E02	116	269	392	467	484	523	591	659
PcOxP_DB02_E03	117	308	369	452	509	566	643	659
PcOxP_DB02_E08	118	269	388	468	490	523	591	659
PcOxP_DB02_E09	110	309	369	452	484	523	644	667
PcOxP_DB02_E11	119	310	377	440	484	567	606	659
PcOxP_DB02_E12	120	311	370	428	484	523	591	656
PcOxP_DB02_F04	121	269	384	467	487	523	591	659
PcOxP_DB02_F06	122	312	392	469	510	568	591	659
PcOxP_DB02_F09	123	289	378	464	484	523	606	659
PcOxP_DB02_F10	9	313	377	428	484	569	645	659
PcOxP_DB02_F11	124	314	416	434	484	523	603	659
PcOxP_DB02_G02	120	289	370	428	484	523	606	659
PcOxP_DB02_G03	125	315	370	428	511	570	628	678
PcOxP_DB02_G04	110	316	369	452	484	571	630	663

Antibody	SEQ ID NO:							
	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB02_G05	126	317	376	428	502	572	591	664
PcOxP_DB02_H02	127	318	417	428	484	523	591	665
PcOxP_DB02_H04	49	319	392	428	484	573	591	670
PcOxP_DB02_H05	128	320	376	428	512	523	646	659
PcOxP_DB02_H06	9	321	377	428	484	574	591	670
PcOxP_DB02_H07	22	322	383	428	484	523	647	667
PcOxP_DB02_H08	129	323	381	428	493	575	591	659
PcOxP_DB02_H09	130	269	383	470	501	523	591	659
PcOxP_DB03_A04	131	324	404	471	484	537	591	659
PcOxP_DB03_A05	132	325	418	428	484	523	635	670
PcOxP_DB03_A06	133	326	383	472	513	576	591	659
PcOxP_DB03_A07	134	327	419	428	484	577	606	659
PcOxP_DB03_A10	53	328	397	428	484	523	648	679
PcOxP_DB03_A12	135	272	372	473	484	523	591	664
PcOxP_DB03_B01	136	329	383	474	484	523	592	659
PcOxP_DB03_B03	4	301	372	428	484	523	591	663
PcOxP_DB03_B06	137	330	420	434	484	523	595	659
PcOxP_DB03_B07	138	269	370	428	514	523	591	659
PcOxP_DB03_B08	1	284	369	428	484	523	591	677
PcOxP_DB03_B09	22	331	383	428	484	523	600	659
PcOxP_DB03_B10	139	269	369	475	484	523	591	659
PcOxP_DB03_B11	140	332	421	436	484	523	649	664
PcOxP_DB03_B12	141	269	378	452	484	523	591	659
PcOxP_DB03_C01	142	333	376	476	515	578	641	659
PcOxP_DB03_C04	143	334	376	428	504	523	591	667
PcOxP_DB03_C08	144	335	422	469	484	523	606	660
PcOxP_DB03_C10	101	298	383	461	484	523	616	659
PcOxP_DB03_D02	1	336	369	428	484	523	650	656
PcOxP_DB03_D03	145	269	369	428	516	523	591	659
PcOxP_DB03_D10	146	337	405	460	484	523	618	659
PcOxP_DB03_D12	147	269	413	431	484	523	591	659
PcOxP_DB03_E03	17	338	382	428	484	579	621	671
PcOxP_DB03_E04	22	320	383	428	484	523	646	659
PcOxP_DB03_E11	4	339	372	428	484	580	591	660
PcOxP_DB03_E12	148	340	406	429	484	527	591	659
PcOxP_DB03_F02	149	341	383	428	517	581	595	659
PcOxP_DB03_F03	150	342	377	437	518	582	640	664
PcOxP_DB03_F05	151	343	369	477	487	583	651	659
PcOxP_DB03_F07	152	344	403	464	484	534	591	659
PcOxP_DB03_F09	94	289	383	459	484	523	606	659
PcOxP_DB03_F11	153	345	369	454	484	584	591	671
PcOxP_DB03_G01	154	346	372	478	519	523	591	680
PcOxP_DB03_G09	155	347	423	429	484	523	591	681

	SEQ ID NO:							
Antibody	VH	VL	CDRH1	CDRH2	CDRH3	CDRL1	CDRL2	CDRL3
PcOxP_DB03_G11	22	348	383	428	484	585	591	659
PcOxP_DB03_G12	89	282	369	434	484	557	591	659
PcOxP_DB03_H02	156	349	382	434	484	523	649	659
PcOxP_DB03_H10	157	296	424	479	484	523	616	660
PcOxP_DB04_A04	158	350	376	429	484	586	591	666
PcOxP_DB04_A05	159	329	425	428	484	523	592	659
PcOxP_DB04_A11	24	351	369	436	484	587	652	659
PcOxP_DB04_B01	160	352	403	428	520	588	638	659
PcOxP_DB04_B07	161	269	417	460	484	523	591	659
PcOxP_DB04_B10	162	353	409	460	484	523	623	664
PcOxP_DB04_B11	163	269	404	452	484	523	591	659
PcOxP_DB04_B12	1	354	369	428	484	523	591	682
PcOxP_DB04_C09	164	355	383	428	521	553	653	659
PcOxP_DB04_C10	165	269	372	480	493	523	591	659
PcOxP_DB04_C11	1	356	369	428	484	523	654	659
PcOxP_DB04_D01	166	357	369	477	484	523	648	659
PcOxP_DB04_D05	167	358	369	481	484	560	591	659
PcOxP_DB04_D07	110	334	369	452	484	523	591	667
PcOxP_DB04_D09	87	359	409	428	484	580	606	659
PcOxP_DB04_D10	168	360	384	452	484	589	593	661
PcOxP_DB04_D12	169	269	377	482	484	523	591	659
PcOxP_DB04_E05	170	269	410	483	484	523	591	659
PcOxP_DB04_E06	171	269	384	428	489	523	591	659
PcOxP_DB04_E08	172	361	426	429	484	523	622	659
PcOxP_DB04_E12	8	362	376	428	484	523	637	676
PcOxP_DB04_F01	173	304	427	428	484	523	591	671
PcOxP_DB04_F03	174	269	373	452	506	523	591	659
PcOxP_DB04_F05	1	363	369	428	484	590	622	659
PcOxP_DB04_G01	175	364	369	429	521	555	591	661
PcOxP_DB04_G03	176	365	405	428	522	523	615	672
PcOxP_DB04_G05	177	269	376	428	510	523	591	659
PcOxP_DB04_G08	178	366	384	428	484	523	626	668
PcOxP_DB04_G09	179	269	410	429	484	523	591	659
PcOxP_DB04_G11	180	367	400	452	484	523	655	659
PcOxP_DB04_H01	89	368	369	434	484	523	606	680

[0067] In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising a VH domain comprising one, two, or all three of the CDRs of a VH domain set forth in Table 1. In certain embodiments, the antibody comprises the CDRH1 of a VH domain set forth in Table 1. In certain embodiments, the antibody comprises the CDRH2

of a VH domain set forth in Table 1. In certain embodiments, the antibody comprises the CDRH3 of a VH domain set forth in Table 1.

[0068] In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising a VL domain comprising one, two, or all three of the CDRs of a VL domain disclosed in Table 1. In certain embodiments, the antibody comprises the CDRL1 of a VL domain set forth in Table 1. In certain embodiments, the antibody comprises the CDRL2 of a VL domain set forth in Table 1. In certain embodiments, the antibody comprises the CDRL3 of a VL domain set forth in Table 1.

[0069] The individual CDRs of an antibody disclosed herein can be determined according to any CDR numbering scheme known in the art.

[0070] In certain embodiments, one or more of the CDRs of an antibody disclosed herein can be determined according to Kabat *et al.*, J. Biol. Chem. 252, 6609-6616 (1977) and Kabat *et al.*, Sequences of protein of immunological interest (1991), each of which is herein incorporated by reference in its entirety.

[0071] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein as determined by the Kabat numbering scheme.

[0072] In certain embodiments, one or more of the CDRs of an antibody disclosed herein can be determined according to the Chothia numbering scheme, which refers to the location of immunoglobulin structural loops (*see, e.g.*, Chothia C & Lesk AM, (1987), J Mol Biol 196: 901-917; Al-Lazikani B *et al.*, (1997) J Mol Biol 273: 927-948; Chothia C *et al.*, (1992) J Mol Biol 227: 799-817; Tramontano A *et al.*, (1990) J Mol Biol 215(1): 175-82; and U.S. Patent No. 7,709,226, all of which are herein incorporated by reference in their entireties).

[0073] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein, as determined by the Chothia numbering system.

[0074] In certain embodiments, one or more of the CDRs of an antibody disclosed herein can be determined according to MacCallum RM *et al.*, (1996) J Mol Biol 262: 732-745, herein incorporated by reference in its entirety. *See also, e.g.*, Martin A. "Protein Sequence and Structure Analysis of Antibody Variable Domains," in *Antibody Engineering*, Kontermann and Dübel, eds.,

Chapter 31, pp. 422-439, Springer-Verlag, Berlin (2001), herein incorporated by reference in its entirety.

[0075] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein, as determined by the MacCallum numbering system.

[0076] In certain embodiments, the CDRs of an antibody disclosed herein can be determined according to the IMGT numbering system as described in: Lefranc M-P, (1999) The Immunologist 7: 132-136; Lefranc M-P *et al.,* (1999) Nucleic Acids Res 27: 209-212, each of which is herein incorporated by reference in its entirety; and Lefranc M-P *et al.,* (2009) Nucleic Acids Res 37: D1006-D1012.

[0077] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein, as determined by the IMGT numbering system.

[0078] In certain embodiments, the CDRs of an antibody disclosed herein can be determined according to the AbM numbering scheme, which refers to AbM hypervariable regions, which represent a compromise between the Kabat CDRs and Chothia structural loops, and are used by Oxford Molecular's AbM antibody modeling software (Oxford Molecular Group, Inc.), herein incorporated by reference in its entirety.

[0079] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein as determined by the AbM numbering scheme.

[0080] In certain embodiments, the CDRs of an antibody disclosed herein can be determined according to the AHo numbering system, as described in Honegger and Plückthun, A., J. Mol. Biol. 309:657-670 (2001), herein incorporated by reference in its entirety.

[0081] In certain embodiments, the instant disclosure provides antibodies that specifically bind to PC and comprise CDRs of an antibody disclosed in Table 1 herein, as determined by the AHo numbering system.

[0082] In certain embodiments, the individual CDRs of an antibody disclosed herein are each independently determined according to one of the Kabat, Chothia, MacCallum, IMGT, AHo, or AbM numbering schemes, or by structural analysis of the molecule, wherein the structural analysis

identifies residues in the variable region(s) predicted to make contact with an epitope region of PC.

[0083] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds PC, comprising a VH comprising the CDRH1, CDRH2, and CDRH3 amino acid sequences of any one of the VH amino acid sequences set forth in SEQ ID NOs: 1-180, and a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences of any one of the VL amino acid sequences set forth in SEQ ID NOs: 181-368, wherein each CDR is independently determined according to one of the Kabat, Chothia, MacCallum, IMGT, AHo, or AbM numbering schemes, or by structural analysis of the molecule, wherein the structural analysis identifies residues in the variable region(s) predicted to make contact with an epitope region of PC.

[0084] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, wherein the antibody or polypeptide comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences of the VH and VL amino acid sequences set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and

284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368, respectively.

[0085] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, wherein the antibody or polypeptide comprises a VH comprising the CDRH1, CDRH2 and CDRH3 amino acid sequences set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499;

384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484, respectively.

[0086] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, wherein the antibody or polypeptide comprises a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662;

523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661;

523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680, respectively.

[0087] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, wherein the antibody or polypeptide comprises a VH comprising CDRH1, CDRH2, and CDRH3 regions, and a VL comprising CDRL1, CDRL2, and CDRL3 regions, wherein the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 regions comprise the amino acid sequences set forth in SEQ ID NOs: 369, 428, 484, 523, 591, and 656; 370, 429, 485, 523, 592, and 657; 371, 428, 486, 523, 593, and 658; 372, 428, 484, 523, 591, and 659; 373, 429, 484, 523, 594, and 659; 369, 428, 484, 523, 591, and 659; 374, 430, 484, 523, 591, and 659; 369, 428, 484, 523, 595, and 660; 375, 428, 487, 523, 596, and 659; 376, 428, 484, 524, 591, and 659; 377, 428, 484, 523, 591, and 661; 378, 428, 484, 523, 591, and 662; 372, 428, 484, 523, 597, and 658; 379, 428, 484, 523, 598, and 662; 372, 428, 488, 525, 599, and 659; 376, 431, 484, 523, 600, and 663; 380, 432, 484, 523, 591, and 664; 372, 428, 489, 523, 601, and 659; 381, 428, 490, 523, 591, and 659; 382, 428, 484, 526, 597, and 665; 381, 428, 491, 523, 602, and 659; 369, 428, 484, 527, 591, and 661; 377, 428, 492, 528, 591, and 662; 376, 433, 484, 529, 603, and 662; 383, 434, 484, 523, 604, and 666; 383, 428, 484, 523, 605, and 667; 384, 435, 484, 530, 606, and 659; 369, 436, 484, 523, 607, and 659; 372, 437, 487, 523, 591, and 659; 372, 428, 484, 523, 608, and 659; 385, 428, 493, 523, 609, and 662; 386, 428, 484, 531, 591, and 663; 372, 437, 484, 523, 608, and 661; 377, 428, 484, 523, 610, and 659; 387, 428, 484, 523, 611, and 668; 385, 428, 484, 523, 611, and 658; 372, 438, 484, 523, 596, and 662; 388, 428, 494, 523, 612, and 667; 369, 439, 484, 523, 613, and 668; 389, 428, 484, 523, 591, and 669; 382, 428, 484, 523, 591, and 663; 369, 428, 484, 523, 614, and 659; 381, 428, 484, 523, 591, and 659; 376, 440, 495, 523, 591, and 659; 381, 428, 484, 532, 615, and 662; 381, 428, 484, 523, 616, and 670; 390, 441, 484, 523, 591, and 659; 370, 442, 484, 523, 591, and 668; 391, 428, 484, 523, 617, and 671; 377, 428, 484, 533, 595, and 659; 377, 428, 484, 523, 618, and 659; 392, 432, 484, 523, 591, and 659; 377, 443, 484, 534, 619, and 662; 376, 428, 484, 535, 620, and 659; 393, 428, 484, 536, 621, and 659; 381, 428, 484, 537, 603, and 671; 383, 444, 489, 523, 622, and 59; 372, 428, 484, 523, 617, and 659; 377, 428, 484, 523, 623, and 659; 376, 428, 484, 538, 607, and 672; 369, 428, 484, 523, 616, and 671; 376, 428, 484, 523, 624, and 659; 394, 428, 484, 523, 591, and 659; 369, 428, 484, 523, 620, and 659; 383, 444, 496, 523, 625, and 660; 385, 428, 484, 523, 602, and 671; 376, 434, 484, 523, 591, and 659; 395, 445, 497, 523, 611, and 663; 396, 446, 487, 523, 626, and 670; 369, 428, 484, 523, 617, and 659;

392, 428, 484, 523, 591, and 662; 394, 428, 484, 523, 606, and 673; 393, 428, 498, 523, 591, and 659; 376, 428, 495, 523, 627, and 671; 369, 440, 484, 523, 628, and 671; 397, 428, 484, 539, 591, and 662; 389, 447, 484, 523, 591, and 659; 398, 448, 492, 523, 591, and 670; 373, 449, 490, 523, 611, and 659; 399, 428, 484, 537, 613, and 671; 400, 450, 484, 540, 598, and 659; 401, 428, 484, 541, 591, and 659; 390, 428, 484, 542, 629, and 659; 376, 428, 484, 523, 591, and 671; 400, 428, 499, 523, 591, and 659; 381, 428, 484, 523, 630, and 667; 384, 429, 484, 543, 631, and 659; 369, 428, 484, 523, 632, and 664; 402, 436, 484, 523, 597, and 661; 381, 451, 484, 523, 591, and 656; 403, 428, 484, 523, 633, and 659; 369, 429, 484, 544, 607, and 659; 404, 429, 484, 523, 630, and 659; 372, 429, 484, 523, 602, and 659; 381, 428, 484, 523, 591, and 665; 388, 428, 484, 523, 610, and 674; 405, 451, 484, 523, 634, and 671; 406, 428, 484, 545, 591, and 661; 400, 428, 484, 523, 635, and 667; 404, 428, 484, 546, 591, and 659; 384, 432, 500, 523, 636, and 664; 376, 452, 501, 547, 591, and 663; 407, 428, 484, 548, 619, and 659; 375, 428, 484, 523, 637, and 659; 372, 428, 484, 523, 607, and 659; 408, 428, 484, 523, 638, and 659; 386, 428, 484, 523, 591, and 659; 369, 428, 497, 523, 591, and 659; 403, 453, 484, 549, 591, and 659; 402, 454, 484, 523, 591, and 659; 383, 428, 484, 523, 591, and 659; 383, 434, 500, 523, 591, and 659; 376, 455, 502, 550, 591, and 675; 383, 435, 484, 523, 591, and 664; 369, 428, 484, 523, 602, and 659; 376, 428, 484, 551, 591, and 659; 376, 428, 484, 552, 591, and 659; 383, 428, 484, 553, 591, and 676; 376, 428, 484, 554, 591, and 659; 376, 428, 490, 523, 591, and 676; 369, 428, 503, 555, 606, and 659; 409, 428, 484, 523, 591, and 659; 383, 428, 504, 556, 591, and 659; 369, 434, 484, 523, 591, and 659; 390, 428, 484, 523, 637, and 677; 369, 456, 484, 523, 591, and 659; 370, 457, 484, 557, 591, and 659; 383, 428, 484, 558, 591, and 659; 404, 458, 499, 523, 591, and 659; 410, 428, 484, 523, 591, and 677; 383, 459, 484, 553, 639, and 659; 407, 428, 489, 549, 591, and 667; 374, 434, 484, 523, 591, and 659; 404, 428, 484, 559, 617, and 666; 411, 460, 505, 523, 591, and 672; 372, 429, 484, 523, 606, and 659; 383, 428, 485, 523, 591, and 659; 386, 460, 490, 523, 601, and 659; 412, 455, 493, 523, 592, and 670; 372, 428, 484, 560, 591, and 667; 372, 428, 484, 523, 606, and 659; 383, 461, 484, 523, 591, and 677; 369, 429, 484, 523, 606, and 659; 369, 434, 484, 530, 591, and 659; 376, 437, 484, 561, 603, and 666; 383, 462, 500, 523, 591, and 659; 383, 428, 484, 562, 591, and 659; 400, 463, 484, 523, 616, and 660; 376, 464, 484, 523, 602, and 677; 400, 434, 506, 549, 591, and 659; 369, 436, 507, 523, 591, and 659; 404, 429, 484, 523, 591, and 659; 384, 429, 484, 523, 616, and 659; 369, 429, 484, 523, 591, and 659; 377, 465, 484, 523, 630, and 660; 413, 459, 484, 563, 591, and 659; 369, 452, 484, 523, 591, and 663; 414, 466, 484, 523, 640, and 659; 373, 428, 484, 523,

591, and 659; 415, 428, 489, 564, 591, and 659; 369, 428, 484, 523, 591, and 671; 400, 428, 484, 523, 641, and 677; 369, 428, 491, 565, 591, and 662; 403, 458, 508, 523, 642, and 664; 392, 467, 484, 523, 591, and 659; 369, 452, 509, 566, 643, and 659; 388, 468, 490, 523, 591, and 659; 369, 452, 484, 523, 644, and 667; 377, 440, 484, 567, 606, and 659; 370, 428, 484, 523, 591, and 656; 384, 467, 487, 523, 591, and 659; 392, 469, 510, 568, 591, and 659; 378, 464, 484, 523, 606, and 659; 377, 428, 484, 569, 645, and 659; 416, 434, 484, 523, 603, and 659; 370, 428, 484, 523, 606, and 659; 370, 428, 511, 570, 628, and 678; 369, 452, 484, 571, 630, and 663; 376, 428, 502, 572, 591, and 664; 417, 428, 484, 523, 591, and 665; 392, 428, 484, 573, 591, and 670; 376, 428, 512, 523, 646, and 659; 377, 428, 484, 574, 591, and 670; 383, 428, 484, 523, 647, and 667; 381, 428, 493, 575, 591, and 659; 383, 470, 501, 523, 591, and 659; 404, 471, 484, 537, 591, and 659; 418, 428, 484, 523, 635, and 670; 383, 472, 513, 576, 591, and 659; 419, 428, 484, 577, 606, and 659; 397, 428, 484, 523, 648, and 679; 372, 473, 484, 523, 591, and 664; 383, 474, 484, 523, 592, and 659; 372, 428, 484, 523, 591, and 663; 420, 434, 484, 523, 595, and 659; 370, 428, 514, 523, 591, and 659; 369, 428, 484, 523, 591, and 677; 383, 428, 484, 523, 600, and 659; 369, 475, 484, 523, 591, and 659; 421, 436, 484, 523, 649, and 664; 378, 452, 484, 523, 591, and 659; 376, 476, 515, 578, 641, and 659; 376, 428, 504, 523, 591, and 667; 422, 469, 484, 523, 606, and 660; 383, 461, 484, 523, 616, and 659; 369, 428, 484, 523, 650, and 656; 369, 428, 516, 523, 591, and 659; 405, 460, 484, 523, 618, and 659; 413, 431, 484, 523, 591, and 659; 382, 428, 484, 579, 621, and 671; 383, 428, 484, 523, 646, and 659; 372, 428, 484, 580, 591, and 660; 406, 429, 484, 527, 591, and 659; 383, 428, 517, 581, 595, and 659; 377, 437, 518, 582, 640, and 664; 369, 477, 487, 583, 651, and 659; 403, 464, 484, 534, 591, and 659; 383, 459, 484, 523, 606, and 659; 369, 454, 484, 584, 591, and 671; 372, 478, 519, 523, 591, and 680; 423, 429, 484, 523, 591, and 681; 383, 428, 484, 585, 591, and 659; 369, 434, 484, 557, 591, and 659; 382, 434, 484, 523, 649, and 659; 424, 479, 484, 523, 616, and 660; 376, 429, 484, 586, 591, and 666; 425, 428, 484, 523, 592, and 659; 369, 436, 484, 587, 652, and 659; 403, 428, 520, 588, 638, and 659; 417, 460, 484, 523, 591, and 659; 409, 460, 484, 523, 623, and 664; 404, 452, 484, 523, 591, and 659; 369, 428, 484, 523, 591, and 682; 383, 428, 521, 553, 653, and 659; 372, 480, 493, 523, 591, and 659; 369, 428, 484, 523, 654, and 659; 369, 477, 484, 523, 648, and 659; 369, 481, 484, 560, 591, and 659; 369, 452, 484, 523, 591, and 667; 409, 428, 484, 580, 606, and 659; 384, 452, 484, 589, 593, and 661; 377, 482, 484, 523, 591, and 659; 410, 483, 484, 523, 591, and 659; 384, 428, 489, 523, 591, and 659; 426, 429, 484, 523, 622, and 659; 376, 428, 484, 523, 637, and 676; 427, 428, 484, 523, 591, and 671; 373,

452, 506, 523, 591, and 659; 369, 428, 484, 590, 622, and 659; 369, 429, 521, 555, 591, and 661; 405, 428, 522, 523, 615, and 672; 376, 428, 510, 523, 591, and 659; 384, 428, 484, 523, 626, and 668; 410, 429, 484, 523, 591, and 659; 400, 452, 484, 523, 655, and 659; or 369, 434, 484, 523, 606, and 680, respectively.

[0088] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising a VH comprising an amino acid sequence that is at least 75%, 80%, 85%, 90%, 95%, or 100% (*e.g.*, at least 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99%) identical to any one of the amino acid sequences set forth in SEQ ID NOs: 1-180. In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising a VH comprising any one of the amino acid sequences set forth in SEQ ID NOs: 1-180. In certain embodiments, the amino acid sequence of the VH consists of any one of the amino acid sequences set forth in SEQ ID NOs: 1-180.

[0089] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising a VL comprising an amino acid sequence that is at least 75%, 80%, 85%, 90%, 95%, or 100% (*e.g.*, at least 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99%) identical to any one of the amino acid sequences set forth in SEQ ID NOs: 181-368. In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising a VL comprising any one of the amino acid sequences set forth in SEQ ID NOs: 181-368. In certain embodiments, the amino acid sequence of the VL consists of any one of the amino acid sequences set forth in SEQ ID NOs: 181-368.

[0090] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising a VH comprising an amino acid sequence that is at least 75%, 80%, 85%, 90%, 95%, or 100% (*e.g.*, at least 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99%) identical to any one of the amino acid sequences set forth in SEQ ID NOs: 1-180, and a VL comprising an amino acid sequence that is at least 75%, 80%, 85%, 90%, 95%, or 100% (*e.g.*, at least 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99%) identical to any one of the amino acid sequences set forth in SEQ ID NOs: 181-368. In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC in, comprising a VH comprising any one of the amino acid sequences set forth in SEQ ID NOs: 1-180, and a VL comprising any one of the amino acid sequences set forth in SEQ ID NOs: 181-368. In certain embodiments, the amino acid sequence of the VH consists of any one of the amino acid sequences set forth in SEQ

ID NOs: 1-180; and the amino acid sequence of the VL consists of any one of the amino acid sequences set forth in SEQ ID NOs: 181-368.

[0091] In certain embodiments, the instant disclosure provides an antibody or polypeptide that specifically binds to PC, comprising the VH and VL amino acid sequences set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338;

22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368, respectively.

[0092] In certain embodiments, the amino acid sequences of VH and VL consist of the amino acid sequences set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110

and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368, respectively.

[0093] Any antibody format can be used in the antibodies disclosed herein. In certain embodiments, the antibody is a single chain antibody or single-chain Fv (scFv). In certain embodiments, the antibody is an scFv fused with an Fc region (scFv-Fc). In certain embodiments, the antibody is a Fab fragment. In certain embodiments, the antibody is a $F(ab')_2$ fragment.

[0094] In certain embodiments, the antibody or polypeptide disclosed herein is a multispecific antibody (*e.g.*, a bispecific antibody) which specifically binds to PC and a second antigen.

[0095] In certain embodiments, the antibody or polypeptide disclosed herein is conjugated to a cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label. In certain embodiments, the cytotoxic agent is able to induce death or destruction of a cell in contact therewith. In certain embodiments, the cytostatic agent is able to prevent or substantially reduce proliferation and/or inhibits the activity or function of a cell in contact therewith. In certain embodiments, the cytotoxic agent or cytostatic agent is a chemotherapeutic agent. In certain embodiments, the radionuclide is selected from the group consisting of the isotopes ^{3}H, ^{14}C, ^{32}P, ^{35}S, ^{36}Cl, ^{51}Cr, ^{57}Co, ^{58}Co, ^{59}Fe, ^{67}Cu, ^{90}Y, ^{99}Tc, ^{111}In, ^{117}Lu, ^{121}I, ^{124}I, ^{125}I, ^{131}I, ^{198}Au, ^{211}At, ^{213}Bi, ^{225}Ac, and ^{186}Re. In certain embodiments, the detectable label comprises a fluorescent moiety or a click chemistry handle.

[0096] Any immunoglobulin (Ig) constant region can be used in the polypeptides and antibodies disclosed herein. In certain embodiments, the Ig region is a human IgG, IgE, IgM, IgD, IgA, or IgY immunoglobulin molecule, any class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2), or any subclass (*e.g.*, IgG_2a and IgG_2b) of immunoglobulin molecule.

[0097] In certain embodiments, the instant disclosure provides a polypeptide (*e.g.*, an antibody) that specifically binds to PC, the polypeptide comprising a heavy chain constant region, optionally selected from the group consisting of human IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2.

[0098] In certain embodiments, the instant disclosure provides a polypeptide (*e.g.*, an antibody) that specifically binds to PC, the polypeptide comprising a heavy chain constant region that is a variant of a wild-type heavy chain constant region, wherein the variant heavy chain constant region binds to an FcγR with lower affinity than the wild-type heavy chain constant region binds to the FcγR.

[0099] In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 683 or 684. In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising a heavy chain constant region consisting of the amino acid sequence of SEQ ID NO: 683 or 684. In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising an IgG_1 heavy chain constant region of any allotype or isoallotype. In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising an IgG_1 heavy chain constant region of an allotype selected from the group consisting of G1m1(a), G1m2(x), G1m3(f), and G1m17(z). *See*, *e.g.*, Jefferis and Lefranc (2009) mAbs 1(4): 332-338.

[00100] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into an Fc region (*e.g.*, a CH2 domain (residues 231-340 of human IgG_1) and/or a CH3 domain (residues 341-447 of human IgG_1), numbered according to the EU numbering system) and/or a hinge region (residues 216-230, numbered according to the EU numbering system) of an antibody described herein, to alter one or more functional properties of the antibody, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity.

[00101] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into the hinge region of an antibody described herein, such that the number of cysteine residues in the hinge region is altered (*e.g.*, increased or decreased) as described in, *e.g.*, U.S. Patent No. 5,677,425, herein incorporated by reference in its entirety. The number of cysteine residues in the hinge region may be altered to, *e.g.*, facilitate assembly of the light and heavy chains, or to alter (*e.g.*, increase or decrease) the stability of the antibody.

[00102] In a specific embodiment, one, two, or more amino acid mutations (*e.g.*, substitutions, insertions, or deletions) are introduced into an IgG constant region, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc fragment) to alter (*e.g.*, decrease or increase) half-life of the antibody *in vivo*. *See, e.g.*, International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631; and U.S. Patent Nos. 5,869,046, 6,121,022, 6,277,375, and 6,165,745, all of which are herein incorporated by reference in their entireties, for examples of mutations that will alter (*e.g.*, decrease or increase) the half-life of an antibody *in vivo*. In certain embodiments, one, two or more amino acid mutations (*e.g.*, substitutions, insertions, or deletions) are introduced into an IgG constant region, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc fragment) to decrease the half-life of the antibody *in vivo*. In other embodiments, one, two or more amino acid mutations (*e.g.*, substitutions, insertions, or deletions) are introduced into an IgG constant region, or FcRn-binding fragment thereof (preferably an Fc or hinge-Fc fragment) to increase the half-life of the antibody *in vivo*. In a specific embodiment, the antibodies may have one or more amino acid mutations (*e.g.*, substitutions) in the second constant (CH2) domain (residues 231-340 of human IgG_1) and/or the third constant (CH3) domain (residues 341-447 of human IgG_1), numbered according to the EU numbering system. In a specific embodiment, the constant region of the IgG_1 of antibody described herein comprises a methionine (M) to tyrosine (Y) substitution in position 252, a serine (S) to threonine (T) substitution in position 254, and a threonine (T) to glutamic acid (E) substitution in position 256, numbered according to the EU numbering system. *See* U.S. Patent No. 7,658,921, which is herein incorporated by reference in its entirety. This type of mutant IgG, referred to as "YTE mutant" has been shown to display fourfold increased half-life as compared to wild-type versions of the same antibody (*see* Dall'Acqua WF *et al.*, (2006) J Biol Chem 281: 23514-24, which is herein incorporated by reference in its entirety). In certain embodiments, an antibody comprises an IgG constant region comprising one, two, three or more amino acid substitutions of amino acid residues at positions 251-257, 285-290, 308-314, 385-389, and 428-436, numbered according to the EU numbering system.

[00103] In certain embodiments, one, two, or more mutations (*e.g.*, amino acid substitutions) are introduced into an Fc region (*e.g.*, a CH2 domain (residues 231-340 of human IgG_1) and/or a CH3 domain (residues 341-447 of human IgG_1), numbered according to the EU numbering system) and/or a hinge region (residues 216-230, numbered according to the EU numbering system) of an antibody described herein, to increase or decrease the affinity of the antibody for an

Fc receptor (*e.g.*, an activated Fc receptor) on the surface of an effector cell. Mutations in the Fc region of an antibody that decrease or increase the affinity of an antibody for an Fc receptor and techniques for introducing such mutations into the Fc receptor or fragment thereof are known to one of skill in the art. Examples of mutations in the Fc receptor of an antibody that can be made to alter the affinity of the antibody for an Fc receptor are described in, *e.g.*, Smith P *et al.*, (2012) PNAS 109: 6181-6186, U.S. Patent No. 6,737,056, and International Publication Nos. WO 02/060919; WO 98/23289; and WO 97/34631, all of which are herein incorporated by reference in their entireties.

[00104] In certain embodiments, the antibody comprises a heavy chain constant region that is a variant of a wild-type heavy chain constant region, wherein the variant heavy chain constant region binds to FcγRIIB with higher affinity than the wild-type heavy chain constant region binds to FcγRIIB. In certain embodiments, the variant heavy chain constant region is a variant human heavy chain constant region, *e.g.*, a variant human IgG_1, a variant human IgG_2, or a variant human IgG_4 heavy chain constant region. In certain embodiments, the variant human IgG heavy chain constant region comprises one or more of the following amino acid mutations, according to the EU numbering system: G236D, P238D, S239D, S267E, L328F, and L328E. In certain embodiments, the variant human IgG heavy chain constant region comprises a set of amino acid mutations selected from the group consisting of: S267E and L328F; P238D and L328E; P238D and one or more substitutions selected from the group consisting of E233D, G237D, H268D, P271G, and A330R; P238D, E233D, G237D, H268D, P271G, and A330R; G236D and S267E; S239D and S267E; V262E, S267E, and L328F; and V264E, S267E, and L328F, according to the EU numbering system. In certain embodiments, the FcγRIIB is expressed on a cell selected from the group consisting of macrophages, monocytes, B cells, dendritic cells, endothelial cells, and activated T cells.

[00105] In a further embodiment, one, two, or more amino acid substitutions are introduced into an IgG constant region Fc region to alter the effector function(s) of the antibody. For example, one or more amino acids selected from amino acid residues 234, 235, 236, 237, 239, 243, 267, 292, 297, 300, 318, 320, 322, 328, 330, 332, and 396, numbered according to the EU numbering system, can be replaced with a different amino acid residue such that the antibody has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of

complement. This approach is described in further detail in U.S. Patent Nos. 5,624,821 and 5,648,260, each of which is herein incorporated by reference in its entirety. In certain embodiments, the deletion or inactivation (through point mutations or other means) of a constant region domain may reduce Fc receptor binding of the circulating antibody thereby increasing tumor localization. *See, e.g.*, U.S. Patent Nos. 5,585,097 and 8,591,886, each of which is herein incorporated by reference in its entirety, for a description of mutations that delete or inactivate the constant region and thereby increase tumor localization. In certain embodiments, one or more amino acid substitutions may be introduced into the Fc region of an antibody described herein to remove potential glycosylation sites on the Fc region, which may reduce Fc receptor binding (*see, e.g.*, Shields RL *et al.*, (2001) J Biol Chem 276: 6591-604, which is herein incorporated by reference in its entirety). In various embodiments, one or more of the following mutations in the constant region of an antibody described herein may be made: an N297A substitution; an N297Q substitution; an L234A substitution; an L234F substitution; an L235A substitution; an L235F substitution; an L235V substitution; an L237A substitution; an S239D substitution; an E233P substitution; an L234V substitution; an L235A substitution; a C236 deletion; a P238A substitution; an S239D substitution; an F243L substitution; a D265A substitution; an S267E substitution; an L328F substitution; an R292P substitution; a Y300L substitution; an A327Q substitution; a P329A substitution; an A330L substitution; an I332E substitution; or a P396L substitution, numbered according to the EU numbering system.

[00106] In certain embodiments, a mutation selected from the group consisting of D265A, P329A, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of L235A, L237A, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S267E, L328F, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S239D, I332E, optionally A330L, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of L235V, F243L, R292P, Y300L, P396L, and a combination thereof, numbered according to the

EU numbering system, may be made in the constant region of an antibody described herein. In certain embodiments, a mutation selected from the group consisting of S267E, L328F, and a combination thereof, numbered according to the EU numbering system, may be made in the constant region of an antibody described herein.

[00107] In a specific embodiment, an antibody described herein comprises the constant region of an IgG_1 with an N297Q or N297A amino acid substitution, numbered according to the EU numbering system. In certain embodiments, an antibody described herein comprises the constant region of an IgG_1 with a mutation selected from the group consisting of D265A, P329A, and a combination thereof, numbered according to the EU numbering system. In another embodiment, an antibody described herein comprises the constant region of an IgG_1 with a mutation selected from the group consisting of L234A, L235A, and a combination thereof, numbered according to the EU numbering system. In another embodiment, an antibody described herein comprises the constant region of an IgG_1 with a mutation selected from the group consisting of L234F, L235F, N297A, and a combination thereof, numbered according to the EU numbering system. In certain embodiments, amino acid residues in the constant region of an antibody described herein in the positions corresponding to positions L234, L235, and D265 in a human IgG_1 heavy chain, numbered according to the EU numbering system, are not L, L, and D, respectively. This approach is described in detail in International Publication No. WO 14/108483, which is herein incorporated by reference in its entirety. In certain embodiments, the amino acids corresponding to positions L234, L235, and D265 in a human IgG_1 heavy chain are F, E, and A; or A, A, and A, respectively, numbered according to the EU numbering system.

[00108] In certain embodiments, one or more amino acids selected from amino acid residues 329, 331, and 322 in the constant region of an antibody described herein, numbered according to the EU numbering system, can be replaced with a different amino acid residue such that the antibody has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Patent No. 6,194,551 (Idusogie *et al.*), which is herein incorporated by reference in its entirety. In certain embodiments, one or more amino acid residues within amino acid positions 231 to 238 in the N-terminal region of the CH2 domain of an antibody described herein are altered to thereby alter the ability of the antibody to fix complement, numbered according to the EU numbering system. This approach is described further in International Publication No. WO 94/29351, which is herein incorporated by reference

in its entirety. In certain embodiments, the Fc region of an antibody described herein is modified to increase the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody for an Fcγ receptor by mutating one or more amino acids (*e.g.*, introducing amino acid substitutions) at the following positions: 238, 239, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, 276, 278, 280, 283, 285, 286, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, 309, 312, 315, 320, 322, 324, 326, 327, 328, 329, 330, 331, 333, 334, 335, 337, 338, 340, 360, 373, 376, 378, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438, or 439, numbered according to the EU numbering system. This approach is described further in International Publication No. WO 00/42072, which is herein incorporated by reference in its entirety.

[00109] In certain embodiments, an antibody described herein comprises a modified constant region of an IgG_1, wherein the modification increases the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC). In certain embodiments, 0.1, 1, or 10 μg/mL of the antibody is capable of inducing cell death of at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, or 60% of PC-expressing cells within 1, 2, or 3 hours, as assessed by methods described herein and/or known to a person of skill in the art. In certain embodiments, the modified constant region of an IgG_1 comprises S239D and I332E substitutions, numbered according to the EU numbering system. In certain embodiments, the modified constant region of an IgG_1 comprises S239D, A330L, and I332E substitutions, numbered according to the EU numbering system. In certain embodiments, the modified constant region of an IgG_1 comprises L235V, F243L, R292P, Y300L, and P396L substitutions, numbered according to the EU numbering system. In certain embodiments, the antibody is capable of inducing cell death in effector T cells and Tregs, wherein the percentage of Tregs that undergo cell death is higher than the percentage of effector T cells that undergo cell death by at least 1.2 fold, 1.3 fold, 1.4 fold, 1.5 fold, 1.6 fold, 1.7 fold, 1.8 fold, 1.9 fold, 2 fold, 2.5 fold, 3 fold, 3.5 fold, 4 fold, 4.5 fold, or 5 fold.

[00110] In certain embodiments, an antibody described herein comprises the constant region of an IgG_4 antibody and the serine at amino acid residue 228 of the heavy chain, numbered according to the EU numbering system, is substituted for proline. In certain embodiments, the instant disclosure provides an antibody that specifically binds to PC, the antibody comprising a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 684.

[00111] In certain embodiments, any of the constant region mutations or modifications described herein can be introduced into one or both heavy chain constant regions of an antibody described herein having two heavy chain constant regions.

Pharmaceutical Compositions

[00112] Provided herein are compositions comprising an anti-PC antibody disclosed herein having the desired degree of purity in a physiologically acceptable carrier, excipient, or stabilizer (*see, e.g.*, Remington's Pharmaceutical Sciences (1990) Mack Publishing Co., Easton, PA). Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates, including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose, or sorbitol; salt-forming counter-ions such as sodium; metal complexes (*e.g.*, Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONIC™ or polyethylene glycol (PEG).

[00113] In a specific embodiment, pharmaceutical compositions comprise an anti-PC antibody disclosed herein, and optionally one or more additional prophylactic or therapeutic agents, in a pharmaceutically acceptable carrier. In a specific embodiment, pharmaceutical compositions comprise an anti-PC antibody disclosed herein, and optionally one or more additional prophylactic or therapeutic agents, in a pharmaceutically acceptable carrier. In certain embodiments, the antibody is the only active ingredient included in the pharmaceutical composition. Pharmaceutical compositions described herein can be useful in decreasing or inhibiting PC activity and treating a condition, such as an inflammatory disorder. In certain embodiments, the present disclosure relates to a pharmaceutical composition of the present disclosure comprising an anti-PC antibody of the present disclosure for use as a medicament. In another embodiment, the present disclosure relates

to a pharmaceutical composition of the present disclosure for use in a method for the treatment of an inflammatory disorder.

[00114] Pharmaceutically acceptable carriers used in parenteral preparations include aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, local anesthetics, suspending and dispersing agents, emulsifying agents, sequestering, or chelating agents and other pharmaceutically acceptable substances. Examples of aqueous vehicles include Sodium Chloride Injection, Ringer's Injection, Isotonic Dextrose Injection, Sterile Water Injection, Dextrose and Lactated Ringer's Injection. Nonaqueous parenteral vehicles include fixed oils of vegetable origin, cottonseed oil, corn oil, sesame oil, and peanut oil. Antimicrobial agents in bacteriostatic or fungistatic concentrations can be added to parenteral preparations packaged in multiple-dose containers which include phenols or cresols, mercurials, benzyl alcohol, chlorobutanol, methyl and propyl p-hydroxybenzoic acid esters, thimerosal, benzalkonium chloride, and benzethonium chloride. Isotonic agents include sodium chloride and dextrose. Buffers include phosphate and citrate. Antioxidants include sodium bisulfate. Local anesthetics include procaine hydrochloride. Suspending and dispersing agents include sodium carboxymethylcellulose, hydroxypropyl methylcellulose, and polyvinylpyrrolidone. Emulsifying agents include Polysorbate 80 (TWEEN® 80). A sequestering or chelating agent of metal ions includes EDTA. Pharmaceutical carriers also include ethyl alcohol, polyethylene glycol, and propylene glycol for water miscible vehicles; and sodium hydroxide, hydrochloric acid, citric acid, or lactic acid for pH adjustment.

[00115] A pharmaceutical composition can be formulated for any route of administration to a subject. Specific examples of routes of administration include intranasal, oral, pulmonary, transdermal, intradermal, and parenteral. Parenteral administration, characterized by either subcutaneous, intramuscular, or intravenous injection, is also contemplated herein. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions. The injectables, solutions, and emulsions also contain one or more excipients. Suitable excipients are, for example, water, saline, dextrose, glycerol, or ethanol. In addition, if desired, the pharmaceutical compositions to be administered can also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents, stabilizers, solubility enhancers, and other such agents,

such as for example, sodium acetate, sorbitan monolaurate, triethanolamine oleate, and cyclodextrins.

[00116] Preparations for parenteral administration of antibody include sterile solutions ready for injection, sterile dry soluble products, such as lyophilized powders, ready to be combined with a solvent just prior to use, including hypodermic tablets, sterile suspensions ready for injection, sterile dry insoluble products ready to be combined with a vehicle just prior to use, and sterile emulsions. The solutions may be either aqueous or nonaqueous.

[00117] If administered intravenously, suitable carriers include physiological saline or phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents, such as glucose, polyethylene glycol, and polypropylene glycol, and mixtures thereof.

[00118] Topical mixtures comprising an antibody are prepared as described for the local and systemic administration. The resulting mixture can be a solution, suspension, emulsion, or the like and can be formulated as creams, gels, ointments, emulsions, solutions, elixirs, lotions, suspensions, tinctures, pastes, foams, aerosols, irrigations, sprays, suppositories, bandages, dermal patches, or any other formulations suitable for topical administration.

[00119] An anti-PC antibody disclosed herein can be formulated as an aerosol for topical application, such as by inhalation (*see, e.g.*, U.S. Patent Nos. 4,044,126, 4,414,209, and 4,364,923, which describe aerosols for delivery of a steroid useful for treatment of inflammatory diseases, particularly asthma and are herein incorporated by reference in their entireties). These formulations for administration to the respiratory tract can be in the form of an aerosol or solution for a nebulizer, or as a microfine powder for insufflations, alone or in combination with an inert carrier such as lactose. In such a case, the particles of the formulation will, in certain embodiments, have diameters of less than 50 microns, in certain embodiments less than 10 microns.

[00120] An anti-PC antibody disclosed herein can be formulated for local or topical application, such as for topical application to the skin and mucous membranes, such as in the eye, in the form of gels, creams, and lotions and for application to the eye or for intracisternal or intraspinal application. Topical administration is contemplated for transdermal delivery and also for administration to the eyes or mucosa, or for inhalation therapies. Nasal solutions of the antibody alone or in combination with other pharmaceutically acceptable excipients can also be administered.

[00121] Transdermal patches, including iontophoretic and electrophoretic devices, are well known to those of skill in the art, and can be used to administer an antibody. For example, such patches are disclosed in U.S. Patent Nos. 6,267,983, 6,261,595, 6,256,533, 6,167,301, 6,024,975, 6,010715, 5,985,317, 5,983,134, 5,948,433, and 5,860,957, all of which are herein incorporated by reference in their entireties.

[00122] In certain embodiments, a pharmaceutical composition comprising an antibody described herein is a lyophilized powder, which can be reconstituted for administration as solutions, emulsions, and other mixtures. It may also be reconstituted and formulated as solids or gels. The lyophilized powder is prepared by dissolving antibody described herein, or a pharmaceutically acceptable derivative thereof, in a suitable solvent. In certain embodiments, the lyophilized powder is sterile. The solvent may contain an excipient which improves the stability or other pharmacological component of the powder or reconstituted solution, prepared from the powder. Excipients that may be used include, but are not limited to, dextrose, sorbitol, fructose, corn syrup, xylitol, glycerin, glucose, sucrose, or other suitable agent. The solvent may also contain a buffer, such as citrate, sodium or potassium phosphate or other such buffer known to those of skill in the art at, in certain embodiments, about neutral pH. Subsequent sterile filtration of the solution followed by lyophilization under standard conditions known to those of skill in the art provides the desired formulation. In certain embodiments, the resulting solution will be apportioned into vials for lyophilization. Each vial will contain a single dosage or multiple dosages of the compound. The lyophilized powder can be stored under appropriate conditions, such as at about 4°C to room temperature. Reconstitution of this lyophilized powder with water for injection provides a formulation for use in parenteral administration. For reconstitution, the lyophilized powder is added to sterile water or other suitable carrier. The precise amount depends upon the selected compound. Such amount can be empirically determined.

[00123] The anti-PC antibodies disclosed herein and other compositions provided herein can also be formulated to be targeted to a particular tissue, receptor, or other area of the body of the subject to be treated. Many such targeting methods are well known to those of skill in the art. All such targeting methods are contemplated herein for use in the instant compositions. For non-limiting examples of targeting methods, *see, e.g.*, U.S. Patent Nos. 6,316,652, 6,274,552, 6,271,359, 6,253,872, 6,139,865, 6,131,570, 6,120,751, 6,071,495, 6,060,082, 6,048,736,

6,039,975, 6,004,534, 5,985,307, 5,972,366, 5,900,252, 5,840,674, 5,759,542, and 5,709,874, all of which are herein incorporated by reference in their entireties.

[00124] The compositions to be used for *in vivo* administration can be sterile. This is readily accomplished by filtration through, *e.g.*, sterile filtration membranes.

Methods of Use and Uses

[00125] In another aspect, the instant disclosure provides a method of treating a subject using the anti-PC antibodies disclosed herein. Any disease or disorder in a subject that would benefit from decrease of oxidized phospholipid function can be treated using the anti-PC antibodies disclosed herein.

[00126] In certain embodiments, the anti-PC antibodies disclosed herein are particularly useful for inhibiting an activity of PC in a subject. In certain embodiments, the anti-PC antibodies disclosed herein are particularly useful for inhibiting the inflammatory activity of PC in a subject. In certain embodiments, the anti-PC antibodies disclosed herein are particularly useful for treating an inflammatory disorder or degenerative disease. In certain embodiments, the anti-PC antibodies disclosed herein can be used as an anti-inflammatory agent and/or as an anti-atherosclerotic agent. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat pain. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat osteoporosis. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat fibrotic disease, including, without limitation, lung fibrosis. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat NETosis-driven diseases, including, without limitation, anti-neutrophil cytoplasmic antibody (ANCA) vasculitis and Type I diabetes. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat chronic obstructive pulmonary disease (COPD). In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat acute respiratory diseases, acute fulminating pneumonias, or other similar disorders. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat severe asthma. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat patients with acute hepatitis, or with non-alcoholic steatohepatitis (NASH) and metabolic syndrome. In certain embodiments, the anti-PC antibodies disclosed herein can be used as an anti-atherosclerotic agent to treat cardiovascular disease and calcific aortic stenosis (CAS). In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat patients with acute coronary syndromes or with "crescendo angina." In certain embodiments, the anti-PC antibodies disclosed herein can be used

as a proactive measure in treating high risk patients, *e.g.*, patients who have a propensity for stroke or developing atherosclerosis. In certain embodiments, the anti-PC antibodies disclosed herein can be used treat high risk patients with coronary artery disease (CAD). Thus, the anti-PC antibodies disclosed herein can be used to treat inflammatory diseases and disorders, cardiovascular diseases, and diseases associated with oxidized phospholipids, including, without limitation, atherosclerosis, acute coronary syndrome, acute myocardial infarction, myocardial infarction (heart attack), stable and unstable angina pectoris, aneurysms, coronary artery disease (CAD), ischemic heart disease, ischemic myocardium, cardiac and sudden cardiac death, cardiomyopathy, congestive heart failure, heart failure, stenosis, peripheral arterial disease (PAD), intermittent claudication, critical limb ischemia, and stroke. *See*, U.S. Patent No. 11,008,381, which is incorporated herein by reference in its entirety.

[00127] In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat cardiovascular disease, atherosclerosis, rheumatoid arthritis, osteoarthritis, lung tissue injury (*e.g.*, caused by smoking), brain lesions, apoptosis, senescence, Crohn's disease, ulcerative colitis, fatty liver disease (*e.g.*, NASH), and non-alcoholic fatty liver disease (NAFLD). Thus, the anti-PC antibodies disclosed herein can be used to treat inflammatory diseases and disorders, cardiovascular diseases, liver diseases and disorder (*e.g.*, NASH, NAFLD) and diseases associated with oxidative stress and damage. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat non-alcoholic fatty liver disease. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat non-alcoholic steatohepatitis (NASH). In certain embodiments, the anti-PC antibodies disclosed herein can be used to inhibit the progression of NAFLD to NASH. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat or inhibit atherogenesis. *See*, U.S. Patent No. 11,168,148, which is incorporated herein by reference in its entirety.

[00128] In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat reperfusion injury. In certain embodiments, reperfusion injury comprises organ reperfusion injury. In certain embodiments, reperfusion injury comprises ischemic-reperfusion injury. In certain embodiments, organ reperfusion injury is induced by an ischemic event (e.g., myocardial infarction induced reperfusion injury). In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat a subject that is at risk of suffering or has suffered an ischemic event, including, without limitation, an ischemic event associated with a condition selected from the

group consisting of cerebral ischemia; intestinal ischemia; spinal cord ischemia; cardiovascular ischemia; myocardial ischemia associated with myocardial infarction; myocardial ischemia associated with congestive heart failure (CHF), ischemia associated with age-related macular degeneration (AME); liver ischemia; kidney/renal ischemia; dermal ischemia; vasoconstriction-induced tissue ischemia; penile ischemia as a consequence of priapism and erectile dysfunction; ischemia associated with thromboembolytic disease; ischemia associated with microvascular disease; ischemia associated with thrombosis; and ischemia associated with diabetic ulcers, gangrenous conditions, post-trauma syndrome, cardiac arrest resuscitation, hypothermia, peripheral nerve damage and neuropathies. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat a subject that is at risk of suffering or has suffered an ischemic event that is the result of an induced injury, including, without limitation, from surgery, transplantation, accidental trauma, and mechanical support devices. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat a subject that is at risk of suffering or has suffered an ischemic event that is the result of heart surgery, kidney surgery, brain surgery, liver surgery, and bypass surgery. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat acute ischemic stroke. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat reperfusion-driven indications including transplantation of organs such as the liver, heart, and kidney. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat a disease associated with thrombosis, including, without limitation sickle cell disease, deep vein thrombosis, pulmonary embolism, cardiac embolism, hypercoagulable state, thrombophilia, Factor V Leiden, Antithrombin III deficiency, Protein C deficiency, Protein S deficiency, Prothrombin gene mutation (G20210A), hyperhomocysteinemia, antiphospholipid antibody syndrome (APS), anticardiolipin antibody (ACLA) thrombosis syndrome, and lupus anticoagulant (LA) syndrome. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat or inhibit atherogenesis. *See*, U.S. Patent Application Serial No. 16/759,331, which is incorporated herein by reference in its entirety.

[00129] In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat a toll-like receptor 2 (TLR2)-mediated disease or disorder, including, without limitation, Kawasaki disease including IVIG-refractory Kawasaki Disease, type 2 diabetes, rheumatoid arthritis, dermatologic disease, multiple sclerosis, systemic lupus erythematosus, ulcerative colitis, Graves'

Disease, Sjögren's syndrome, autoimmune thyroid diseases, or vasculitis. *See*, U.S. Patent Application Serial No. 16/965,271, which is incorporated herein by reference in its entirety.

[00130] In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat bacterial infection. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat neuroinflammatory diseases, including, without limitation, amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and Alzheimer's disease (AD). In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat Huntington's disease, frontotemporal dementia (FTD), multiple sclerosis (MS), clinically isolated syndrome (CIS), and other demyelinating diseases of the central nervous system. In certain embodiments, the anti-PC antibodies disclosed herein can be used to treat ocular disease, including, without limitation, age-related macular degeneration (AMD) and geographic atrophy (GA).

[00131] In certain embodiments, these methods further comprise administering an additional therapeutic agent to the subject. In certain embodiments, the additional therapeutic agent is a HMG-CoA reductase inhibitor (statin), immunosuppressive agent, ezetimide, perixosome, nicotinic acid, squalene inhibitor, proliferative activated receptor (PPAR) agonist, cholesteryl ester transfer protein (CETP) inhibitor, ApoA-1 Milano, corticosteroid, non-steroidal anti-inflammatory drug, steroidal anti-inflammatory drug, analgesic, growth factor, anti-atherosclerosis drug, anti-proliferative agent, HSP, Beta-2-glycoprotein-I, and any derivative and analog thereof.

[00132] HMGCoA reductase inhibitors (statins) are well-known drugs that effectively reduce low-density lipoprotein (LDL)-cholesterol levels by inhibiting the enzyme that regulates the rate of cholesterol production and increasing the clearance of LDL-cholesterol (LDL-C) present in the blood by the liver. Non-limiting examples of commonly prescribed statins include Atorvastatin, Fluvastatin, Lovastatin, Pravastatin, and Simvastatin.

[00133] Non-limiting examples of immunosuppressive agents include biologics such as infliximab, abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, ixekizumab, natalizumab, rituximab, secukinumab, tocilizumab, ustekinumab, canakinumab, and vedolizumab, calcineurin inhibitors such as cyclosporine and tacrolimus, mTOR inhibitors such as sirolimus and everolimus, inosine monophosphate dehydrogenase (IMDH) inhibitors such as azathioprine, leflunomide, and mycophenolate, methotrexate, monoclonal antibodies such as daclizumab and basiliximab, muromonab-CD3, and Janus kinase inhibitors such as tofacitinib.

[00134] Ezetimibe is the first of a new class of cholesterol absorption inhibitors that potently and selectively inhibits dietary and biliary cholesterol absorption at the brush border of the intestinal epithelium, without affecting the absorption of triglyceride or fat-soluble vitamins. Ezetimibe thus reduces overall cholesterol delivery to the liver, secondarily inducing increased expression of LDL receptors, resulting in an increased removal of LDL-C from the plasma.

[00135] The peroxisome is a single-membrane organelle present in nearly all eukaryotic cells. One of the most important metabolic processes of the peroxisome is the β-oxidation of long and very long chain fatty acids. The peroxisome is also involved in bile acid synthesis, cholesterol synthesis, plasmalogen synthesis, amino acid metabolism, and purine metabolism.

[00136] Nicotinic acid is a known agent that lowers total cholesterol, LDL-cholesterol, and triglyceride levels, while raising high-density lipoprotein (HDL)-cholesterol levels. There are three types of nicotinic acid drugs: immediate release, timed release, and extended release. Nicotinic acid or niacin, the water-soluble B vitamin, improves all lipoproteins when given in doses well above the vitamin requirement.

[00137] Squalene, an isoprenoid compound structurally similar to beta-carotene, is an intermediate metabolite in the synthesis of cholesterol. In humans, about 60 percent of dietary squalene is absorbed. It is transported in serum generally in association with very low-density lipoproteins and is distributed ubiquitously in human tissues, with the greatest concentration in the skin, where it is one of the major components of skin surface lipids. Squalene inhibitors (*e.g.*, monooxygenase and synthase) serve as cholesterol biosynthesis inhibitors.

[00138] Proliferative Activated Receptor (PPAR) agonists, *e.g.*, fibrates, are fatty acid-activated members of the nuclear receptor superfamily that play important roles in lipid and glucose metabolism, and have been implicated in obesity-related metabolic diseases such as hyperlipidemia, insulin resistance, and coronary artery disease. Fibrates are generally effective in lowering elevated plasma triglycerides and cholesterol and act as PPAR agonists. The most pronounced effect of fibrates includes a decrease in plasma triglyceride-rich lipoproteins (TRLs). Levels of LDL-C generally decrease in individuals with elevated baseline plasma concentrations, and HDL cholesterol (HDL-C) levels are usually increased when baseline plasma concentrations are low. Non-limiting examples of commonly prescribed fibrates include bezafibrate, gemfibrozil, and fenofibrate.

[00139] Cholesteryl Ester Transfer Protein (CETP) inhibitors play a major role in atherogenesis, by reducing cholesteryl ester accumulation within macrophages and the arterial wall, and thus reducing foam cell formation and affecting the cholesterol absorption. The most promising presently known CETP inhibitor is avisimibe.

[00140] ApoA-1 Milano is typically used as a recombinant complex with phospholipid (ETC-216) and produces significant regression of coronary atherosclerosis.

[00141] Non-limiting examples of non-steroidal anti-inflammatory drugs include oxicams, such as piroxicam, isoxicam, tenoxicam, sudoxicam, and CP-14,304; salicylates, such as aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal; acetic acid derivatives, such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acematacin, fentiazac, zomepirac, clindanac, oxepinac, felbinac, and ketorolac; fenamates, such as mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acids; propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indopropfen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic; pyrazoles, such as phenylbutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

[00142] Non-limiting examples of steroidal anti-inflammatory drugs include, without limitation, corticosteroids such as hydrocortisone, hydroxyltriamcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionates, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylesters, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone, fludrocortisone, difluorosone diacetate, fluradrenolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, diflurprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, triamcinolone, and mixtures thereof.

[00143] Non-limiting examples of analgesics (pain relievers) include aspirin and other salicylates (such as choline or magnesium salicylate), ibuprofen, ketoprofen, naproxen sodium, and acetaminophen.

[00144] Growth factors are hormones which have numerous functions, including regulation of adhesion molecule production, altering cellular proliferation, increasing vascularization, enhancing collagen synthesis, regulating bone metabolism, and altering migration of cells into given area. Non-limiting examples of growth factors include insulin-like growth factor-1 (IGF-1), transforming growth factor-β (TGF-β), a bone morphogenic protein (BMP), and the like.

[00145] Non-limiting examples of anti-proliferative agents include an alkylating agent such as a nitrogen mustard, an ethylenimine and a methylmelamine, an alkyl sulfonate, a nitrosourea, and a triazene; an antimetabolite such as a folic acid analog, a pyrimidine analog, and a purine analog; a natural product such as a vinca alkaloid, an epipodophyllotoxin, an antibiotic, an enzyme, a taxane, and a biological response modifier, miscellaneous agents such as a platinum coordination complex, an anthracenedione, an anthracycline, a substituted urea, a methyl hydrazine derivative, or an adrenocortical suppressant; or a hormone or an antagonist such as an adrenocorticosteroid, a progestin, an estrogen, an antiestrogen, an androgen, an antiandrogen, or a gonadotropin-releasing hormone analog. Specific examples of chemotherapeutic agents include, for example, a nitrogen mustard, an epipodophyllotoxin, an antibiotic, a platinum coordination complex, bleomycin, doxorubicin, paclitaxel, etoposide, 4-OH cyclophosphamide, and cisplatinum.

[00146] The HSP family consists of approximately 25 proteins discerned by their molecular weights with highly conserved structures. Almost all humans have cellular and humoral immune reactions against microbial heat-shock protein 60 (HSP60). Because a high degree of antigenic homology exists between microbial (bacterial and parasitic) and human HSP60, the 'cost' of immunity to microbes might be the danger of cross-reactivity with human HSP60 expressed by the endothelial cells of stressed arteries. Genuine autoimmunity against altered autologous HSP60 might trigger this process also (Wick et al., TRENDS in Immunology. 2001; 22(12):665-669). HSP has been implicated as a target autoantigen in several experimental autoimmune diseases (arthritis, type I diabetes). Anti-HSP65 as well as anti-HSP60 antibodies have been demonstrably associated with atheromatous lesions in humans. Studies conducted in rabbits and mice show that the generation of an HSP65-induced immune response by immunization with the recombinant protein or with an HSP65-rich preparation of *Mycobacterium tuberculosis* enhances

atherogenesis. As autoimmune processes pointing to HSP65 as a possible antigenic candidate, creating a state of unresponsiveness by induction of mucosal "tolerization" has been employed in order to block these responses, our group reported that early atherosclerosis was attenuated in HSP65-fed mice, compared with either BSA or PBS fed mice (Harats et al., J Am Coll Cardiol. 2002; 40:1333-1338), this was further supported by Maron who demonstrated that nasal vaccination with HSP reduces the inflammatory process associated with atherosclerosis (Maron et al., Circulation. 2002; 106:1708-1715).

[00147] Beta-2-glycoprotein I (beta2GPI) is a phospholipid binding protein shown to serve as a target for prothrombotic anti-phospholipid antibodies. It has recently been demonstrated to drive an immune mediated reaction and enhance murine atherosclerosis. β-Antibodies to beta-2-GPI have the ability to activate monocytes and endothelial cells and can induce an immune response to beta2GPI in atherosclerosis-prone mice accelerated atherosclerosis. When beta2GPI-reactive lymph node and spleen cells were transferred to LDL-receptor-deficient mice they promoted fatty streak formation, proving a direct proatherogenic role for beta2GPI-specific lymphocytes. Inducing immunological tolerance to beta2GPI by prior oral feeding with the antigen resulted in a significant reduction in the extent of atherosclerotic lesions. Thus, beta2GPI is a candidate player in the atherosclerotic plaque, and can possibly be employed as an immunomodulator of plaque progression. Oral feeding with of beta2GPI inhibited lymph node cell reactivity to beta2GPI in mice immunized against the human protein. IL-4 and IL-10 production was upregulated in lymph node cells of beta2GPI-tolerant mice immunized against beta2GPI, upon priming with the respective protein. Thus, oral administration of beta2GPI is an effective means of suppressing atherogenesis in mice (George et al., Cardiovasc Res. 2004; 62(3):603-9).

[00148] In certain embodiments, the anti-PC antibodies or pharmaceutical compositions disclosed herein synergize with the additional therapeutic agent.

[00149] In certain embodiments, the present disclosure relates to an antibody and/or pharmaceutical composition of the present disclosure for use in a method of the present disclosure, wherein the method further comprises administering an additional therapeutic agent to the subject. In certain embodiments, the present disclosure relates to (a) an antibody and/or pharmaceutical composition of the present disclosure, and (b) an additional therapeutic agent for use as a medicament. In certain embodiments, the present disclosure relates to (a) an antibody and/or pharmaceutical composition of the present disclosure, and (b) an additional therapeutic agent for

use in a method for the treatment of an inflammatory disorder. In a further embodiment, the present disclosure relates to a pharmaceutical composition, kit or kit-of-parts comprising (a) an antibody and/or pharmaceutical composition of the present disclosure, and (b) an additional therapeutic agent. In certain embodiments, the additional therapeutic agent is an HMG-CoA reductase inhibitor (statin), immunosuppressive agent, ezetimibe, peroxisome, nicotinic acid, squalene inhibitor, proliferative activated receptor (PPAR) agonist, cholesteryl ester transfer protein (CETP) inhibitor, ApoA-1 Milano, non-steroidal anti-inflammatory drug, steroidal anti-inflammatory drug, analgesic, growth factor, anti-atherosclerosis drug, anti-proliferative agent, HSP, or Beta-2-glycoprotein-I.

[00150] The anti-PC antibody and the additional therapeutic agent (*e.g.*, HMG-CoA reductase inhibitor (statin), immunosuppressive agent, ezetimibe, peroxisome, nicotinic acid, squalene inhibitor, proliferative activated receptor (PPAR) agonist, cholesteryl ester transfer protein (CETP) inhibitor, ApoA-1 Milano, non-steroidal anti-inflammatory drug, steroidal anti-inflammatory drug, analgesic, growth factor, anti-atherosclerosis drug, anti-proliferative agent, HSP, or Beta-2-glycoprotein-I) can be administered separately, sequentially, or concurrently as separate dosage forms.

[00151] An antibody or pharmaceutical composition described herein may be delivered to a subject by a variety of routes. These include, but are not limited to, parenteral, intranasal, intratracheal, oral, intradermal, topical, intramuscular, intraperitoneal, transdermal, intravenous, intratumoral, conjunctival, intra-arterial, and subcutaneous routes. Pulmonary administration can also be employed, *e.g.*, by use of an inhaler or nebulizer, and formulation with an aerosolizing agent for use as a spray. In certain embodiments, the antibody or pharmaceutical composition described herein is delivered subcutaneously or intravenously. In certain embodiments, the antibody or pharmaceutical composition described herein is delivered intra-arterially. In certain embodiments, the antibody or pharmaceutical composition described herein is delivered intratumorally. In certain embodiments, the antibody or pharmaceutical composition described herein is delivered into a tumor draining lymph node.

[00152] The amount of an antibody or composition which will be effective in the treatment and/or prevention of a condition will depend on the nature of the disease, and can be determined by standard clinical techniques.

[00153] The precise dose to be employed in a composition will also depend on the route of administration, and the seriousness of the infection or disease caused by it, and should be decided according to the judgment of the practitioner and each subject's circumstances. For example, effective doses may also vary depending upon means of administration, target site, physiological state of the patient (including age, body weight, and health), whether the patient is human or an animal, other medications administered, or whether treatment is prophylactic or therapeutic. Usually, the patient is a human, but non-human mammals, including transgenic mammals, can also be treated. Treatment dosages are optimally titrated to optimize safety and efficacy.

[00154] An anti-PC antibody described herein can also be used to assay OxPL levels in a biological sample using classical immunohistological methods known to those of skill in the art, including immunoassays, such as the enzyme linked immunosorbent assay (ELISA), immunoprecipitation, or Western blotting. Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{125}I, ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^{3}H), indium (^{121}In), and technetium (^{99}Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin. Such labels can be used to label an antibody described herein. Alternatively, a second antibody that recognizes an anti-PC antibody described herein can be labeled and used in combination with an anti-PC antibody to detect OxPL levels. Therefore, in certain embodiments, the present disclosure relates to the use of an anti-PC antibody of the present disclosure for *in vitro* detection of OxPL in a biological sample. In a further embodiment, the present disclosure relates to the use of an anti-PC antibody of the disclosure, for assaying and/or detecting OxPL levels in a biological sample *in vitro* or *ex vivo*, optionally wherein the anti-PC antibody is conjugated to a radionuclide or detectable label, and/or carries a label described herein, and/or wherein an immunohistological method is used.

[00155] Assaying for the level of OxPL is intended to include qualitatively or quantitatively measuring or estimating the level of OxPL in a first biological sample either directly (*e.g.*, by determining or estimating absolute OxPL level) or relatively (*e.g.*, by comparing to the disease associated OxPL level in a second biological sample). OxPL level in the first biological sample can be measured or estimated and compared to a standard OxPL level, the standard being taken, for example, from a second biological sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having

the disorder. As will be appreciated in the art, once the "standard" OxPL level is known, it can be used repeatedly as a standard for comparison. Therefore, in a further embodiment, the present disclosure relates to an *in vitro* method for assaying and/or detecting OxPL levels, for example human OxPL levels, in a biological sample, comprising qualitatively or quantitatively measuring or estimating the level of OxPL, for example of human OxPL, in a biological sample, by an immunohistological method.

[00156] As used herein, the term "biological sample" refers to any biological sample obtained from a subject, cell line, tissue, or other source of cells potentially containing oxidized phospholipids. Methods for obtaining tissue biopsies and body fluids from animals (*e.g.*, humans or cynomolgus monkeys) are well known in the art. Biological samples include peripheral blood mononuclear cells (PBMCs).

[00157] An anti-PC antibody described herein can be used for prognostic, diagnostic, monitoring, and screening applications, including *in vitro* and *in vivo* applications well known and standard to the skilled artisan and based on the present description. Prognostic, diagnostic, monitoring, and screening assays and kits for *in vitro* assessment and evaluation of immune system status and/or immune response may be utilized to predict, diagnose, and monitor to evaluate patient samples, including those known to have or suspected of having an immune system dysfunction or with regard to an anticipated or desired immune system response or antigen response. The assessment and evaluation of immune system status and/or immune response is also useful in determining the suitability of a patient for a clinical trial of a drug or for the administration of a particular therapeutic agent or antibody, including combinations thereof, versus a different agent or antibody. *In vivo* applications include directed cell therapy and immune system modulation and radio imaging of immune responses. Therefore, in certain embodiments, the present disclosure relates to an anti-PC antibody and/or pharmaceutical composition of the present disclosure for use as a diagnostic. In certain embodiments, the present disclosure relates to an anti-PC antibody and/or pharmaceutical composition of the present disclosure for use in a method for the prediction, diagnosis, and/or monitoring of a subject having or suspected to have an immune system dysfunction and/or with regard to an anticipated or desired immune system response or antigen response. In another embodiment, the present disclosure relates to the use of an anti-PC antibody of the disclosure, for predicting, diagnosing, and/or monitoring of a subject having or suspected to have an immune system dysfunction and/or with regard to an anticipated or desired immune

system response or antigen response, by assaying and/or detecting human OxPL levels in a biological sample of the subject *in vitro* or *in vivo*.

[00158] In certain embodiments, an anti-PC antibody can be used in immunohistochemistry of biopsy samples. In certain embodiments, the method is an *in vitro* method. In another embodiment, an anti-PC antibody can be used to detect levels of OxPL, or levels of cells which contain OxPL, the levels of which can then be linked to certain disease symptoms. Anti-PC antibodies described herein may carry a detectable or functional label and/or may be conjugated to a radionuclide or detectable label. When fluorescence labels are used, currently available microscopy and fluorescence-activated cell sorter analysis (FACS) or combination of both methods procedures known in the art may be utilized to identify and to quantitate the specific binding members. Anti-PC antibodies described herein may carry or may be conjugated to a fluorescence label. Exemplary fluorescence labels include, for example, reactive and conjugated probes, *e.g.*, Aminocoumarin, Fluorescein and Texas red, Alexa Fluor dyes, Cy dyes and DyLight dyes. An anti-PC antibody may carry or may be conjugated to a radioactive label or radionuclide, such as the isotopes ^{3}H, ^{14}C, ^{32}P, ^{35}S, ^{36}Cl, ^{51}Cr, ^{57}Co, ^{58}Co, ^{59}Fe, ^{67}Cu, ^{90}Y, ^{99}Tc, ^{111}In, ^{117}Lu, ^{121}I, ^{124}I, ^{125}I, ^{131}I, ^{198}Au, ^{211}At, ^{213}Bi, ^{225}Ac, and ^{186}Re. When radioactive labels are used, currently available counting procedures known in the art may be utilized to identify and quantitate the specific binding of an anti-PC antibody to PC. In the instance where the label is an enzyme, detection may be accomplished by any of the presently utilized colorimetric, spectrophotometric, fluorospectrophotometric, amperometric, or gasometric techniques as known in the art. This can be achieved by contacting a sample or a control sample with an anti-PC antibody under conditions that allow for the formation of a complex between the anti-PC antibody and PC. Any complexes formed between the anti-PC antibody and PC, are detected and compared in the sample and the control. In light of the specific binding of the anti-PC antibodies described herein for PC, the anti-PC antibodies can be used to specifically detect PC. The anti-PC antibodies described herein can also be used to purify PC via immunoaffinity purification. Also included herein is an assay system which may be prepared in the form of a test kit, kit, or kit-of-parts for the quantitative analysis of the extent of the presence of, for instance, PC/PC ligand complexes. The system, test kit, kit, or kit-of-parts may comprise a labeled component, *e.g.*, a labeled antibody, and one or more additional immunochemical reagents.

Polynucleotides, Vectors, and Methods of Producing Antibodies

[00159] In another aspect, provided herein are polynucleotides comprising a nucleotide sequence encoding an antibody, or a portion thereof, described herein or a fragment thereof (*e.g.*, a VL and/or VH; and a light chain and/or heavy chain) that specifically binds to a PC antigen, and vectors, *e.g.*, vectors comprising such polynucleotides for recombinant expression in host cells (*e.g.*, *E. coli* and mammalian cells). Provided herein are polynucleotides comprising nucleotide sequences encoding a heavy and/or light chain of any of the antibodies provided herein, as well as vectors comprising such polynucleotide sequences, *e.g.*, expression vectors for their efficient expression in host cells, *e.g.*, mammalian cells.

[00160] As used herein, an "isolated" polynucleotide or nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source (*e.g.*, in a mouse or a human) of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. For example, the language "substantially free" includes preparations of polynucleotide or nucleic acid molecules having less than about 15%, 10%, 5%, 2%, 1%, 0.5%, or 0.1% (in particular less than about 10%) of other material, *e.g.*, cellular material, culture medium, other nucleic acid molecules, chemical precursors, and/or other chemicals. In a specific embodiment, a nucleic acid molecule(s) encoding an antibody described herein is isolated or purified.

[00161] In particular aspects, provided herein are polynucleotides comprising nucleotide sequences encoding antibodies, which specifically bind to PC and comprises an amino acid sequence as described herein, as well as antibodies which compete with such antibodies for binding to PC (*e.g.*, in a dose-dependent manner), or which binds to the same epitope as that of such antibodies.

[00162] In certain aspects, provided herein are polynucleotides comprising a nucleotide sequence encoding the light chain or heavy chain of antibody described herein. The polynucleotides can comprise nucleotide sequences encoding a light chain comprising the VL FRs and CDRs of antibodies described herein (*see, e.g.*, Table 1) or nucleotide sequences encoding a heavy chain comprising the VH FRs and CDRs of antibodies described herein (*see, e.g.*, Table 1). In certain embodiments, a polynucleotide encodes a VH, VL, heavy chain, and/or light chain of a

described herein. In another embodiment, a polynucleotide encodes the first VH and the first VL of a described herein. In another embodiment, a polynucleotide encodes the second VH and the second VL of a described herein. In another embodiment, a polynucleotide encodes the first heavy chain and the first light chain of a described herein. In another embodiment, a polynucleotide encodes the second heavy chain and the second light chain of a described herein. In another embodiment, a polynucleotide encodes the VH and/or the VL, or the heavy chain and/or the light chain, of an antibody described herein.

[00163] Also provided herein are polynucleotides encoding an anti-PC antibody that are optimized, *e.g.*, by codon/RNA optimization, replacement with heterologous signal sequences, and elimination of mRNA instability elements. Methods to generate optimized nucleic acids encoding an anti-PC antibody or a fragment thereof (*e.g.*, light chain, heavy chain, VH domain, or VL domain) for recombinant expression by introducing codon changes and/or eliminating inhibitory regions in the mRNA can be carried out by adapting the optimization methods described in, *e.g.*, U.S. Patent Nos. 5,965,726; 6,174,666; 6,291,664; 6,414,132; and 6,794,498, accordingly, all of which are herein incorporated by reference in their entireties. For example, potential splice sites and instability elements (*e.g.*, A/T or A/U rich elements) within the RNA can be mutated without altering the amino acids encoded by the nucleic acid sequences to increase stability of the RNA for recombinant expression. The alterations utilize the degeneracy of the genetic code, *e.g.*, using an alternative codon for an identical amino acid. In certain embodiments, it can be desirable to alter one or more codons to encode a conservative mutation, *e.g.*, a similar amino acid with similar chemical structure and properties and/or function as the original amino acid. Such methods can increase expression of an anti-PC antibody or fragment thereof by at least 1 fold, 2 fold, 3 fold, 4 fold, 5 fold, 10 fold, 20 fold, 30 fold, 40 fold, 50 fold, 60 fold, 70 fold, 80 fold, 90 fold, or 100 fold or more relative to the expression of an anti-PC antibody encoded by polynucleotides that have not been optimized.

[00164] In certain embodiments, an optimized polynucleotide sequence encoding an anti-PC antibody described herein or a fragment thereof (*e.g.*, VL domain and/or VH domain) can hybridize to an antisense (*e.g.*, complementary) polynucleotide of an unoptimized polynucleotide sequence encoding an anti-PC antibody described herein or a fragment thereof (*e.g.*, VL domain and/or VH domain). In specific embodiments, an optimized nucleotide sequence encoding an anti-PC antibody described herein or a fragment hybridizes under high stringency conditions to

antisense polynucleotide of an unoptimized polynucleotide sequence encoding an anti-PC antibody described herein or a fragment thereof. In a specific embodiment, an optimized nucleotide sequence encoding an anti-PC antibody described herein or a fragment thereof hybridizes under high stringency, intermediate, or lower stringency hybridization conditions, to an antisense polynucleotide of an unoptimized nucleotide sequence encoding an anti-PC antibody described herein or a fragment thereof. Information regarding hybridization conditions has been described, *see, e.g.*, U.S. Patent Application Publication No. US 2005/0048549 (*e.g.*, paragraphs 72-73), which is herein incorporated by reference in its entirety.

[00165] The polynucleotides can be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. Nucleotide sequences encoding antibodies described herein, *e.g.*, antibodies described in Table 1, and modified versions of these antibodies can be determined using methods well known in the art, *i.e.*, nucleotide codons known to encode particular amino acids are assembled in such a way to generate a nucleic acid that encodes the antibody. Such a polynucleotide encoding the antibody can be assembled from chemically synthesized oligonucleotides (*e.g.*, as described in Kutmeier G *et al.*, (1994), BioTechniques 17: 242-6, herein incorporated by reference in its entirety), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing, and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

[00166] Alternatively, a polynucleotide encoding an antigen-binding region of a described here or an antibody described herein can be generated from nucleic acid from a suitable source (*e.g.*, a hybridoma) using methods well known in the art (*e.g.*, PCR and other molecular cloning methods). For example, PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of a known sequence can be performed using genomic DNA obtained from hybridoma cells producing the antibody of interest. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the light chain and/or heavy chain of an antibody. Such PCR amplification methods can be used to obtain nucleic acids comprising the sequence encoding the variable light chain region and/or the variable heavy chain region of an antibody. The amplified nucleic acids can be cloned into vectors for expression in host cells and for further cloning.

[00167] If a clone containing a nucleic acid encoding a particular antigen-binding region or antibody is not available, but the sequence of the antigen-binding region or antibody molecule is

known, a nucleic acid encoding the immunoglobulin can be chemically synthesized or obtained from a suitable source (*e.g.*, an antibody cDNA library or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody described herein) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence, or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, *e.g.*, a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR can then be cloned into replicable cloning vectors using any method well known in the art.

[00168] DNA encoding anti-PC antibodies described herein can be readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the anti-PC antibodies). Hybridoma cells can serve as a source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as *E. coli* cells, simian COS cells, Chinese hamster ovary (CHO) cells (*e.g.*, CHO cells from the CHO GS System™ (Lonza)), or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of anti-PC antibodies in the recombinant host cells.

[00169] To generate whole antibodies or antigen-binding regions, PCR primers including VH or VL nucleotide sequences, a restriction site, and a flanking sequence to protect the restriction site can be used to amplify the VH or VL sequences in scFv clones. Utilizing cloning techniques known to those of skill in the art, the PCR amplified VH domains can be cloned into vectors expressing a heavy chain constant region, *e.g.*, the human gamma 1 or human gamma 4 constant region, and the PCR amplified VL domains can be cloned into vectors expressing a light chain constant region, *e.g.*, human kappa or lambda constant regions. In certain embodiments, the vectors for expressing the VH or VL domains comprise an EF-1α promoter, a secretion signal, a cloning site for the variable region, constant regions, and a selection marker such as neomycin. The VH and VL domains can also be cloned into one vector expressing the necessary constant regions. The heavy chain conversion vectors and light chain conversion vectors are then co-transfected into cell lines to generate stable or transient cell lines that express full-length antibodies, *e.g.*, IgG, using techniques known to those of skill in the art.

[00170] The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant regions in place of the murine sequences, or by covalently

joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide.

[00171] Also provided are polynucleotides that hybridize under high stringency, intermediate, or lower stringency hybridization conditions, to polynucleotides that encode an antibody described herein. In specific embodiments, polynucleotides described herein hybridize under high stringency, intermediate, or lower stringency hybridization conditions, to polynucleotides encoding a VH domain and/or VL domain provided herein.

[00172] Hybridization conditions have been described in the art and are known to one of skill in the art. For example, hybridization under stringent conditions can involve hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC) at about 45°C followed by one or more washes in 0.2xSSC/0.1% SDS at about 50-65°C; hybridization under highly stringent conditions can involve hybridization to filter-bound nucleic acid in 6xSSC at about 45°C followed by one or more washes in 0.1xSSC/0.2% SDS at about 68°C. Hybridization under other stringent hybridization conditions is known to those of skill in the art and have been described, *see, for example*, Ausubel FM *et al.,* eds., (1989) Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York at pages 6.3.1-6.3.6 and 2.10.3, which is herein incorporated by reference in its entirety.

[00173] In certain aspects, provided herein are cells (*e.g.*, host cells) expressing (*e.g.*, recombinantly) antibodies described herein which specifically bind to PC, and related polynucleotides and expression vectors. Provided herein are vectors (*e.g.*, expression vectors) comprising polynucleotides comprising nucleotide sequences encoding anti-PC antibodies or a fragment for recombinant expression in host cells, preferably in mammalian cells (*e.g.*, CHO cells). Also provided herein are host cells comprising such vectors for recombinantly expressing anti-PC antibodies described herein (*e.g.*, human or humanized antibody). In a particular aspect, provided herein are methods for producing an antibody described herein, comprising expressing the antibody from a host cell.

[00174] Recombinant expression of an antibody described herein (*e.g.*, a full-length antigen-binding region or antibody or heavy and/or light chain of an antibody described herein) that specifically binds to PC generally involves construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule, heavy and/or light chain of an antibody, or a fragment thereof (*e.g.*, heavy and/or light chain

variable regions) described herein has been obtained, the vector for the production of the antibody molecule can be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody or antibody fragment (*e.g.*, light chain or heavy chain) encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing an antibody or antibody fragment (*e.g.*, light chain or heavy chain) coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Also provided are replicable vectors comprising a nucleotide sequence encoding containing an antibody molecule described herein, a heavy or light chain of an antibody, a heavy or light chain variable region of an antibody or a fragment thereof, or a heavy or light chain CDR, operably linked to a promoter. Such vectors can, for example, include the nucleotide sequence encoding the constant region of the antibody molecule (*see, e.g.*, International Publication Nos. WO 86/05807 and WO 89/01036; and U.S. Patent No. 5,122,464, which are herein incorporated by reference in their entireties) and variable regions of the antibody can be cloned into such a vector for expression of the entire heavy, the entire light chain, or both the entire heavy and light chains.

[00175] In certain embodiments, a vector comprises a polynucleotide encoding a VH, VL, heavy chain, and/or light chain of an antibody described herein. In another embodiment, a vector comprises a polynucleotide encoding the VH and the VL of an antibody described herein. In another embodiment, a vector comprises a polynucleotide encoding the heavy chain and the light chain of an antibody described herein.

[00176] An expression vector can be transferred to a cell (*e.g.*, host cell) by conventional techniques and the resulting cells can then be cultured by conventional techniques to produce containing an antibody described herein or a fragment thereof. Thus, provided herein are host cells containing a polynucleotide encoding containing an antibody described herein or fragments thereof, or a heavy or light chain thereof, or fragment thereof, or a single-chain antibody described herein, operably linked to a promoter for expression of such sequences in the host cell.

[00177] In another embodiment, a host cell comprises a polynucleotide encoding the VH and VL of an antibody described herein. In another embodiment, a host cell comprises a vector comprising a polynucleotide encoding the VH and VL of an antibody described herein. In another

embodiment, a host cell comprises a first polynucleotide encoding the VH of an antibody described herein, and a second polynucleotide encoding the VL of an antibody described herein. In another embodiment, a host cell comprises a first vector comprising a first polynucleotide encoding the VH of an antibody described herein, and a second vector comprising a second polynucleotide encoding the VL of an antibody described herein.

[00178] In specific embodiments, a heavy chain/heavy chain variable region expressed by a first cell is associated with a light chain/light chain variable region of a second cell to form an anti-PC antibody described herein. In certain embodiments, provided herein is a population of host cells comprising such first host cell and such second host cell.

[00179] In certain embodiments, provided herein is a population of vectors comprising a first vector comprising a polynucleotide encoding a light chain/light chain variable region of an anti-PC antibody described herein, and a second vector comprising a polynucleotide encoding a heavy chain/heavy chain variable region of an anti-PC antibody described herein.

[00180] A variety of host-expression vector systems can be utilized to express antibody molecules described herein (*see, e.g.*, U.S. Patent No. 5,807,715, which is herein incorporated by reference in its entirety). Such host-expression systems represent vehicles by which the coding sequences of interest can be produced and subsequently purified, but also represent cells which can, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule described herein *in situ*. These include but are not limited to microorganisms such as bacteria (*e.g.*, *E. coli* and *B. subtilis*) transformed with, *e.g.*, recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (*e.g.*, *Saccharomyces* and *Pichia*) transformed with, *e.g.*, recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with, *e.g.*, recombinant virus expression vectors (*e.g.*, baculovirus) containing antibody coding sequences; plant cell systems (*e.g.*, green algae such as *Chlamydomonas reinhardtii*) infected with, *e.g.*, recombinant virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with, *e.g.*, recombinant plasmid expression vectors (*e.g.*, Ti plasmid) containing antibody coding sequences; or mammalian cell systems (*e.g.*, COS (*e.g.*, COS1 or COS), CHO, BHK, MDCK, HEK 293, NS0, PER.C6, VERO, CRL7O3O, HsS78Bst, HeLa, and NIH 3T3, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, and BMT10 cells) harboring, *e.g.*, recombinant expression constructs containing promoters derived from the genome

of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the adenovirus late promoter; the vaccinia virus 7.5K promoter). In a specific embodiment, cells for expressing antibodies described herein are Chinese hamster ovary (CHO) cells, for example CHO cells from the CHO GS System™ (Lonza). In certain embodiments, the heavy chain and/or light chain of an antibody produced by a CHO cell may have an N-terminal glutamine or glutamate residue replaced by pyroglutamate. In certain embodiments, cells for expressing antibodies described herein are human cells, *e.g.*, human cell lines. In a specific embodiment, a mammalian expression vector is pOptiVEC™ or pcDNA3.3. In certain embodiments, bacterial cells such as *Escherichia coli*, or eukaryotic cells (*e.g.*, mammalian cells), especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as CHO cells, in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus, are an effective expression system for antibodies (Foecking MK & Hofstetter H (1986) Gene 45: 101-5; and Cockett MI *et al.,* (1990) Biotechnology 8(7): 662-7, each of which is herein incorporated by reference in its entirety). In certain embodiments, antibodies described herein are produced by CHO cells or NS0 cells. In a specific embodiment, the expression of nucleotide sequences encoding antibodies described herein which specifically bind to PC is regulated by a constitutive promoter, inducible promoter, or tissue specific promoter.

[00181] In bacterial systems, a number of expression vectors can be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such an antibody is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified can be desirable. Such vectors include, but are not limited to, the *E. coli* expression vector pUR278 (Ruether U & Mueller-Hill B (1983) EMBO J 2: 1791-1794), in which the coding sequence can be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye S & Inouye M (1985) Nuc Acids Res 13: 3101-3109; Van Heeke G & Schuster SM (1989) J Biol Chem 24: 5503-5509); and the like, all of which are herein incorporated by reference in their entireties. For example, pGEX vectors can also be used to express foreign polypeptides as fusion proteins with glutathione 5-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione agarose beads followed by elution in

the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

[00182] In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV), for example, can be used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The coding sequence can be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

[00183] In mammalian host cells, a number of viral-based expression systems can be utilized. In cases where an adenovirus is used as an expression vector, the coding sequence of interest can be ligated to an adenovirus transcription/translation control complex, *e.g.*, the late promoter and tripartite leader sequence. This chimeric gene can then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (*e.g.*, region El or E3) will result in a recombinant virus that is viable and capable of expressing the molecule in infected hosts (*see, e.g.*, Logan J & Shenk T (1984) PNAS 81(12): 3655-9, which is herein incorporated by reference in its entirety). Specific initiation signals can also be required for efficient translation of inserted coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression can be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (*see, e.g.*, Bitter G *et al.*, (1987) Methods Enzymol. 153: 516-544, which is herein incorporated by reference in its entirety).

[00184] In addition, a host cell strain can be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (*e.g.*, glycosylation) and processing (*e.g.*, cleavage) of protein products can be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product can be used. Such mammalian host cells include but are not

limited to CHO, VERO, BHK, Hela, MDCK, HEK 293, NIH 3T3, W138, BT483, Hs578T, HTB2, BT2O and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL7O3O, COS (*e.g.*, COS1 or COS), PER.C6, VERO, HsS78Bst, HEK-293T, HepG2, SP210, R1.1, B-W, L-M, BSC1, BSC40, YB/20, BMT10, and HsS78Bst cells. In certain embodiments, anti-PC antibodies described herein are produced in mammalian cells, such as CHO cells.

[00185] In a specific embodiment, the antibodies described herein have reduced fucose content or no fucose content. Such antibodies can be produced using techniques known one skilled in the art. For example, the antibodies can be expressed in cells deficient or lacking the ability of to fucosylate. In a specific example, cell lines with a knockout of both alleles of α1,6-fucosyltransferase can be used to produce antibodies with reduced fucose content. The Potelligent® system (Lonza) is an example of such a system that can be used to produce antibodies with reduced fucose content.

[00186] For long-term, high-yield production of recombinant proteins, stable expression cells can be generated. For example, cell lines which stably express an anti-PC antibody described herein can be engineered. In specific embodiments, a cell provided herein stably expresses a light chain/light chain variable region and a heavy chain/heavy chain variable region which associate to form an antigen-binding region or an antibody described herein.

[00187] In certain aspects, rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (*e.g.*, promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA/polynucleotide, engineered cells can be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method can advantageously be used to engineer cell lines which express an anti-PC described herein or a fragment thereof. Such engineered cell lines can be particularly useful in screening and evaluation of compositions that interact directly or indirectly with the antibody molecule.

[00188] A number of selection systems can be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler M *et al.*, (1977) Cell 11(1): 223-32), hypoxanthineguanine

phosphoribosyltransferase (Szybalska EH & Szybalski W (1962) PNAS 48(12): 2026-2034) and adenine phosphoribosyltransferase (Lowy I *et al.*, (1980) Cell 22(3): 817-23) genes in tk-, hgprt- or aprt-cells, respectively, all of which are herein incorporated by reference in their entireties. Also, antimetabolite resistance can be used as the basis of selection for the following genes: *dhfr*, which confers resistance to methotrexate (Wigler M *et al.*, (1980) PNAS 77(6): 3567-70; O'Hare K *et al.*, (1981) PNAS 78: 1527-31); *gpt*, which confers resistance to mycophenolic acid (Mulligan RC & Berg P (1981) PNAS 78(4): 2072-6); neo, which confers resistance to the aminoglycoside G-418 (Wu GY & Wu CH (1991) Biotherapy 3: 87-95; Tolstoshev P (1993) Ann Rev Pharmacol Toxicol 32: 573-596; Mulligan RC (1993) Science 260: 926-932; and Morgan RA & Anderson WF (1993) Ann Rev Biochem 62: 191-217; Nabel GJ & Felgner PL (1993) Trends Biotechnol 11(5): 211-5); and *hygro*, which confers resistance to hygromycin (Santerre RF *et al.*, (1984) Gene 30(1-3): 147-56), all of which are herein incorporated by reference in their entireties. Methods commonly known in the art of recombinant DNA technology can be routinely applied to select the desired recombinant clone and such methods are described, for example, in Ausubel FM *et al.*, (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler M, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli NC *et al.*, (eds.), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colbère-Garapin F *et al.*, (1981) J Mol Biol 150: 1-14, all of which are herein incorporated by reference in their entireties.

[00189] The expression levels of an antibody molecule can be increased by vector amplification (for a review, *see* Bebbington CR & Hentschel CCG, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol. 3 (Academic Press, New York, 1987), which is herein incorporated by reference in its entirety). When a marker in the vector system is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the gene of interest, production of the protein will also increase (Crouse GF *et al.*, (1983) Mol Cell Biol 3: 257-66, which is herein incorporated by reference in its entirety).

[00190] The host cell can be co-transfected with two or more expression vectors described herein, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors can contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. The host cells can be co-transfected

with different amounts of the two or more expression vectors. For example, host cells can be transfected with any one of the following ratios of a first expression vector and a second expression vector: about 1:1, 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:12, 1:15, 1:20, 1:25, 1:30, 1:35, 1:40, 1:45, or 1:50.

[00191] Alternatively, a single vector can be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot NJ (1986) Nature 322: 562-565; and Köhler G (1980) PNAS 77: 2197-2199, each of which is herein incorporated by reference in its entirety). The coding sequences for the heavy and light chains can comprise cDNA or genomic DNA. The expression vector can be monocistronic or multicistronic. A multicistronic nucleic acid construct can encode 2, 3, 4, 5, 6, 7, 8, 9, 10, or more genes/nucleotide sequences, or in the range of 2-5, 5-10, or 10-20 genes/nucleotide sequences. For example, a bicistronic nucleic acid construct can comprise, in the following order, a promoter, a first gene (*e.g.*, heavy chain of an antibody described herein), and a second gene and (*e.g.*, light chain of an antibody described herein). In such an expression vector, the transcription of both genes can be driven by the promoter, whereas the translation of the mRNA from the first gene can be by a cap-dependent scanning mechanism and the translation of the mRNA from the second gene can be by a cap-independent mechanism, *e.g.*, by an IRES.

[00192] Once an antibody molecule described herein has been produced by recombinant expression, it can be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (*e.g.*, ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the antibodies described herein can be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

[00193] In specific embodiments, an antibody described herein is isolated or purified. In certain embodiments, an isolated antibody is one that is substantially free of other antibodies with different antigenic specificities than the isolated antibody. For example, in certain embodiments, a preparation of an antibody described herein is substantially free of cellular material and/or chemical precursors. The language "substantially free of cellular material" includes preparations of an antibody in which the antibody is separated from cellular components of the cells from which

it is isolated or recombinantly produced. Thus, an antibody that is substantially free of cellular material includes preparations of antibody having less than about 30%, 20%, 10%, 5%, 2%, 1%, 0.5%, or 0.1% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein") and/or variants of an antibody, for example, different post-translational modified forms of an antibody or other different versions of an antibody (*e.g.*, antibody fragments). When the antibody is recombinantly produced, it is also generally substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, 2%, 1%, 0.5%, or 0.1% of the volume of the protein preparation. When the antibody is produced by chemical synthesis, it is generally substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the antibody have less than about 30%, 20%, 10%, or 5% (by dry weight) of chemical precursors or compounds other than the antibody of interest. In a specific embodiment, antibodies described herein are isolated or purified.

[00194] Anti-PC antibodies or fragments thereof can be produced by any method known in the art for the synthesis of proteins or antibodies, for example, by chemical synthesis or by recombinant expression techniques. The methods described herein employ, unless otherwise indicated, conventional techniques in molecular biology, microbiology, genetic analysis, recombinant DNA, organic chemistry, biochemistry, PCR, oligonucleotide synthesis and modification, nucleic acid hybridization, and related fields within the skill of the art. These techniques are described, for example, in the references cited herein and are fully explained in the literature. *See, e.g.*, Maniatis T *et al.*, (1982) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press; Sambrook J *et al.*, (1989), Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press; Sambrook J *et al.*, (2001) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY; Ausubel FM *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons (1987 and annual updates); Current Protocols in Immunology, John Wiley & Sons (1987 and annual updates) Gait (ed.) (1984) Oligonucleotide Synthesis: A Practical Approach, IRL Press; Eckstein (ed.) (1991) Oligonucleotides and Analogues: A Practical Approach, IRL Press; Birren B *et al.*, (eds.) (1999) Genome Analysis: A Laboratory Manual, Cold Spring Harbor Laboratory Press, all of which are herein incorporated by reference in their entireties.

[00195] In a specific embodiment, an antibody described herein is prepared, expressed, created, or isolated by any means that involves creation, *e.g.*, via synthesis, genetic engineering of DNA sequences. In certain embodiments, such an antibody comprises sequences (*e.g.*, DNA sequences or amino acid sequences) that do not naturally exist within the antibody germline repertoire of an animal or mammal (*e.g.*, human) *in vivo*.

[00196] In one aspect, provided herein is a method of making an anti-PC antibody comprising culturing a cell or host cell described herein. In certain embodiments, the method is performed *in vitro*. In a certain aspect, provided herein is a method of making an anti-PC antibody comprising expressing (*e.g.*, recombinantly expressing) the antibody using a cell or host cell described herein (*e.g.*, a cell or a host cell comprising polynucleotides encoding an antibody described herein). In certain embodiments, the cell is an isolated cell. In certain embodiments, the exogenous polynucleotides have been introduced into the cell. In certain embodiments, the method further comprises the step of purifying the antibody obtained from the cell or host cell.

[00197] In certain embodiments, an antibody is produced by expressing in a cell a polynucleotide encoding the VH and VL of an antibody described herein under suitable conditions so that the polynucleotides are expressed and the antibody is produced. In another embodiment, an antibody is produced by expressing in a cell a polynucleotide encoding the heavy chain and light chain of an antibody described herein under suitable conditions so that the polynucleotides are expressed and the antibody is produced. In certain embodiments, an antibody is produced by expressing in a cell a first polynucleotide encoding the VH of an antibody described herein, and a second polynucleotide encoding the VL of an antibody described herein, under suitable conditions so that the polynucleotides are expressed and the antibody is produced. In certain embodiments, an antibody is produced by expressing in a cell a first polynucleotide encoding the heavy chain of an antibody described herein, and a second polynucleotide encoding the light chain of an antibody described herein, under suitable conditions so that the polynucleotides are expressed and the antibody is produced.

[00198] Methods for producing polyclonal antibodies are known in the art (*see, for example*, Chapter 11 in: Short Protocols in Molecular Biology, (2002) 5th Ed., Ausubel FM *et al.*, eds., John Wiley and Sons, New York, which is herein incorporated by reference in its entirety).

[00199] Monoclonal antibodies can be prepared using a wide variety of techniques known in the art, including the use of hybridoma, recombinant, and phage display technologies, or a

combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques, including those known in the art and taught, for example, in Harlow E & Lane D, Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling GJ *et al.,* in: Monoclonal Antibodies and T-Cell Hybridomas 563 681 (Elsevier, N.Y., 1981), each of which is herein incorporated by reference in its entirety. The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. For example, monoclonal antibodies can be produced recombinantly from host cells exogenously expressing an antibody described herein or a fragment thereof, for example, light chain and/or heavy chain of such antibody.

[00200] In specific embodiments, a "monoclonal antibody," as used herein, is an antibody produced by a single cell (*e.g.*, hybridoma or host cell producing a recombinant antibody), wherein the antibody specifically binds to PC as determined, *e.g.*, by ELISA or other antigen-binding or competitive binding assay known in the art, or in the examples provided herein. In certain embodiments, a monoclonal antibody can be a chimeric antibody or a humanized antibody. In certain embodiments, a monoclonal antibody is a monovalent antibody or multivalent (*e.g.*, bivalent) antibody. In certain embodiments, a monoclonal antibody is a monospecific or multispecific antibody (*e.g.*, bispecific antibody). Monoclonal antibodies described herein can, for example, be made by the hybridoma method as described in Kohler G & Milstein C (1975) Nature 256: 495, which is herein incorporated by reference in its entirety, or can, *e.g.*, be isolated from phage libraries using the techniques as described herein, for example. Other methods for the preparation of clonal cell lines and of monoclonal antibodies expressed thereby are well known in the art (*see, for example*, Chapter 11 in: Short Protocols in Molecular Biology, (2002) 5th Ed., Ausubel FM *et al., supra*).

[00201] As used herein, an antibody binds to an antigen multivalently (*e.g.*, bivalently) when the antibody comprises at least two (*e.g.*, two or more) monovalent binding regions, each monovalent binding region capable of binding to an epitope on the antigen. Each monovalent binding region can bind to the same or different epitopes on the antigen.

[00202] Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. For example, in the hybridoma method, a mouse or other appropriate host animal, such as a sheep, goat, rabbit, rat, hamster, or macaque monkey, is immunized to elicit lymphocytes that produce or are capable of producing antibodies that will

specifically bind to the protein (*e.g.*, PC) used for immunization. Alternatively, lymphocytes may be immunized *in vitro*. Lymphocytes then are fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding JW (ed.), Monoclonal Antibodies: Principles and Practice, pp. 59-103 (Academic Press, 1986), herein incorporated by reference in its entirety). Additionally, a RIMMS (repetitive immunization multiple sites) technique can be used to immunize an animal (Kilpatrick KE *et al.*, (1997) Hybridoma 16:381-9, herein incorporated by reference in its entirety).

[00203] In certain embodiments, mice (or other animals, such as rats, monkeys, donkeys, pigs, sheep, hamster, or dogs) can be immunized with an antigen (*e.g.*, PC) and once an immune response is detected, *e.g.*, antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well-known techniques to any suitable myeloma cells, for example, cells from cell line SP20 available from the American Type Culture Collection (ATCC®) (Manassas, VA), to form hybridomas. Hybridomas are selected and cloned by limited dilution. In certain embodiments, lymph nodes of the immunized mice are harvested and fused with NS0 myeloma cells.

[00204] The hybridoma cells thus prepared are seeded and grown in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

[00205] Specific embodiments employ myeloma cells that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. Among these myeloma cell lines are murine myeloma lines, such as the NS0 cell line or those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, CA, USA, and SP-2 or X63-Ag8.653 cells available from the American Type Culture Collection, Rockville, MD, USA. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor D (1984) J Immunol 133: 3001-5; Brodeur *et al.*, Monoclonal Antibody Production Techniques and Applications, pp. 51-63 (Marcel Dekker, Inc., New York, 1987), each of which is herein incorporated by reference in its entirety).

[00206] Culture medium in which hybridoma cells are growing is assayed for production of monoclonal antibodies directed against PC. The binding specificity of monoclonal antibodies produced by hybridoma cells is determined by methods known in the art, for example, immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA).

[00207] After hybridoma cells are identified that produce antibodies of the desired specificity, affinity, and/or activity, the clones may be subcloned by limiting dilution procedures and grown by standard methods (Goding JW (ed.), Monoclonal Antibodies: Principles and Practice, *supra*). Suitable culture media for this purpose include, for example, D-MEM or RPMI 1640 medium. In addition, the hybridoma cells may be grown *in vivo* as ascites tumors in an animal.

[00208] The monoclonal antibodies secreted by the subclones are suitably separated from the culture medium, ascites fluid, or serum by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

[00209] Antibodies described herein include, *e.g.*, antibody fragments which recognize PC, and can be generated by any technique known to those of skill in the art. For example, Fab and $F(ab')_2$ fragments described herein can be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce $F(ab')_2$ fragments). A Fab fragment corresponds to one of the two identical arms of an antibody molecule and contains the complete light chain paired with the VH and CH1 domains of the heavy chain. A $F(ab')_2$ fragment contains the two antigen-binding arms of an antibody molecule linked by disulfide bonds in the hinge region.

[00210] Further, the antibodies described herein can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In particular, DNA sequences encoding VH and VL domains are amplified from animal cDNA libraries (*e.g.*, human or murine cDNA libraries of affected tissues). The DNA encoding the VH and VL domains are recombined together with an scFv linker by PCR and cloned into a phagemid vector. The vector is electroporated in *E. coli*, and the *E. coli* is infected with helper phage. Phage used in these methods are typically filamentous phage, including fd and M13, and the VH and VL domains are usually recombinantly fused to either the phage gene III or gene VIII.

Phage expressing an antigen-binding region that binds to a particular antigen can be selected or identified with antigen, *e.g.*, using labeled antigen or antigen bound or captured to a solid surface or bead. Examples of phage display methods that can be used to make the antibodies described herein include those disclosed in Brinkman U *et al.*, (1995) J Immunol Methods 182: 41-50; Ames RS *et al.*, (1995) J Immunol Methods 184: 177-186; Kettleborough CA *et al.*, (1994) Eur J Immunol 24: 952-958; Persic L *et al.*, (1997) Gene 187: 9-18; Burton DR & Barbas CF (1994) Advan Immunol 57: 191-280; PCT Application No. PCT/GB91/001134; International Publication Nos. WO 90/02809, WO 91/10737, WO 92/01047, WO 92/18619, WO 93/1 1236, WO 95/15982, WO 95/20401, and WO 97/13844; and U.S. Patent Nos. 5,698,426, 5,223,409, 5,403,484, 5,580,717, 5,427,908, 5,750,753, 5,821,047, 5,571,698, 5,427,908, 5,516,637, 5,780,225, 5,658,727, 5,733,743, and 5,969,108, all of which are herein incorporated by reference in their entireties.

[00211] As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen-binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, *e.g.*, as described below. Techniques to recombinantly produce antibody fragments such as Fab, Fab' and $F(ab')_2$ fragments can also be employed using methods known in the art such as those disclosed in PCT publication No. WO 92/22324; Mullinax RL *et al.*, (1992) BioTechniques 12(6): 864-9; Sawai H *et al.*, (1995) Am J Reprod Immunol 34: 26-34; and Better M *et al.*, (1988) Science 240: 1041-1043, all of which are herein incorporated by reference in their entireties.

[00212] In certain embodiments, to generate whole antibodies, PCR primers including VH or VL nucleotide sequences, a restriction site, and a flanking sequence to protect the restriction site can be used to amplify the VH or VL sequences from a template, *e.g.*, scFv clones. Utilizing cloning techniques known to those of skill in the art, the PCR amplified VH domains can be cloned into vectors expressing a VH constant region, and the PCR amplified VL domains can be cloned into vectors expressing a VL constant region, *e.g.*, human kappa or lambda constant regions. Human kappa and lambda constant region sequences are known to those of skill in the art. Examples of human kappa and lambda constant region sequences are set forth in SEQ ID NOs: 688-693. The VH and VL domains can also be cloned into one vector expressing the necessary constant regions. The heavy chain conversion vectors and light chain conversion vectors are then

co-transfected into cell lines to generate stable or transient cell lines that express full-length antibodies, *e.g.*, IgG, using techniques known to those of skill in the art.

[00213] A chimeric antibody is a molecule in which different portions of the antibody are derived from different immunoglobulin molecules. For example, a chimeric antibody can contain a variable region of a mouse or rat monoclonal antibody fused to a constant region of a human antibody. Methods for producing chimeric antibodies are known in the art. *See, e.g.*, Morrison SL (1985) Science 229: 1202-7; Oi VT & Morrison SL (1986) BioTechniques 4: 214-221; Gillies SD *et al.*, (1989) J Immunol Methods 125: 191-202; and U.S. Patent Nos. 5,807,715, 4,816,567, 4,816,397, and 6,331,415, all of which are herein incorporated by reference in their entireties.

[00214] A humanized antibody is capable of binding to a predetermined antigen and which comprises a framework region having substantially the amino acid sequence of a human immunoglobulin and CDRs having substantially the amino acid sequence of a non-human immunoglobulin (*e.g.*, a murine immunoglobulin). In certain embodiments, a humanized antibody also comprises at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. The antibody also can include the CH1, hinge, CH2, CH3, and CH4 regions of the heavy chain. A humanized antibody can be selected from any class of immunoglobulins, including IgM, IgG, IgD, IgA, and IgE, and any isotype, including IgG_1, IgG_2, IgG_3, and IgG_4. Humanized antibodies can be produced using a variety of techniques known in the art, including but not limited to, CDR-grafting (European Patent No. EP 239400; International Publication No. WO 91/09967; and U.S. Patent Nos. 5,225,539, 5,530,101, and 5,585,089), veneering or resurfacing (European Patent Nos. EP 592106 and EP 519596; Padlan EA (1991) Mol Immunol 28(4/5): 489-498; Studnicka GM *et al.*, (1994) Prot Engineering 7(6): 805-814; and Roguska MA *et al.*, (1994) PNAS 91: 969-973), chain shuffling (U.S. Patent No. 5,565,332), and techniques disclosed in, *e.g.*, U.S. Pat. No. 6,407,213, U.S. Pat. No. 5,766,886, International Publication No. WO 93/17105; Tan P *et al.*, (2002) J Immunol 169: 1119-25; Caldas C *et al.*, (2000) Protein Eng. 13(5): 353-60; Morea V *et al.*, (2000) Methods 20(3): 267-79; Baca M *et al.*, (1997) J Biol Chem 272(16): 10678-84; Roguska MA *et al.*, (1996) Protein Eng 9(10): 895 904; Couto JR *et al.*, (1995) Cancer Res. 55 (23 Supp): 5973s-5977s; Couto JR *et al.*, (1995) Cancer Res 55(8): 1717-22; Sandhu JS (1994) Gene 150(2): 409-10; and Pedersen JT *et al.*, (1994) J Mol Biol 235(3): 959-73, all of which are herein incorporated by reference in their entireties. *See also*,

U.S. Application Publication No. US 2005/0042664 A1 (Feb. 24, 2005) and International Publication No. WO 2008/020079, which are herein incorporated by reference in their entireties.

[00215] Methods for making multispecific antibodies (*e.g.*, bispecific antibodies) have been described, *see, for example*, U.S. Patent Nos. 7,951,917; 7,183,076; 8,227,577; 5,837,242; 5,989,830; 5,869,620; 6,132,992; and 8,586,713, all of which are herein incorporated by reference in their entireties.

[00216] Bispecific, bivalent antibodies, and methods of making them, are described, for instance in U.S. Pat. Nos. 5,731,168, 5,807,706, 5,821,333, and U.S. Appl. Publ. Nos. 2003/020734 and 2002/0155537; each of which is herein incorporated by reference in its entirety. Bispecific tetravalent antibodies, and methods of making them are described, for instance, in Int. Appl. Publ. Nos. WO 02/096948 and WO 00/44788, the disclosures of both of which are herein incorporated by reference in its entirety. *See generally*, Int. Appl. Publ. Nos. WO 93/17715, WO 92/08802, WO 91/00360, and WO 92/05793; Tutt *et al.*, J. Immunol. 147:60-69 (1991); U.S. Pat. Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; and 5,601,819; and Kostelny *et al.*, J. Immunol. 148:1547-1553 (1992); each of which is herein incorporated by reference in its entirety.

[00217] A bispecific antibody as described herein can be generated according to the DuoBody technology platform (Genmab A/S) as described, *e.g.*, in International Publication Nos. WO 2011/131746, WO 2011/147986, WO 2008/119353, and WO 2013/060867, and in Labrijn AF *et al.*, (2013) PNAS 110(13): 5145-5150. The DuoBody technology can be used to combine one half of a first monospecific antibody, or first antigen-binding region, containing two heavy and two light chains with one half of a second monospecific antibody, or second antigen-binding region, containing two heavy and two light chains. The resultant heterodimer contains one heavy chain and one light chain from the first antibody, or first antigen-binding region, paired with one heavy chain and one light chain from the second antibody, or second antigen-binding region. When both of the monospecific antibodies, or antigen-binding regions, recognize different epitopes on different antigens, the resultant heterodimer is a bispecific antibody.

[00218] The DuoBody technology requires that each of the monospecific antibodies, or antigen-binding regions includes a heavy chain constant region with a single point mutation in the CH3 domain. The point mutations allow for a stronger interaction between the CH3 domains in the resultant bispecific antibody than between the CH3 domains in either of the monospecific antibodies, or antigen-binding regions. The single point mutation in each monospecific antibody,

or antigen-binding region, is at residue 366, 368, 370, 399, 405, 407, or 409, numbered according to the EU numbering system, in the CH3 domain of the heavy chain constant region, as described, *e.g.*, in International Publication No. WO 2011/131746. Moreover, the single point mutation is located at a different residue in one monospecific antibody, or antigen-binding region, as compared to the other monospecific antibody, or antigen-binding region. For example, one monospecific antibody, or antigen-binding region, can comprise the mutation F405L (*i.e.*, a mutation from phenylalanine to leucine at residue 405), while the other monospecific antibody, or antigen-binding region, can comprise the mutation K409R (*i.e.*, a mutation from lysine to arginine at residue 409), numbered according to the EU numbering system. The heavy chain constant regions of the monospecific antibodies, or antigen-binding regions, can be an IgG_1, IgG_2, IgG_3, or IgG_4 isotype (*e.g.*, a human IgG_1 isotype), and a bispecific antibody produced by the DuoBody technology can retain Fc-mediated effector functions.

[00219] Another method for generating bispecific antibodies has been termed the "knobs-into-holes" strategy (*see, e.g.*, Intl. Publ. WO2006/028936). The mispairing of Ig heavy chains is reduced in this technology by mutating selected amino acids forming the interface of the CH3 domains in IgG. At positions within the CH3 domain at which the two heavy chains interact directly, an amino acid with a small side chain (hole) is introduced into the sequence of one heavy chain and an amino acid with a large side chain (knob) into the counterpart interacting residue location on the other heavy chain. In some embodiments, compositions of the disclosure have immunoglobulin chains in which the CH3 domains have been modified by mutating selected amino acids that interact at the interface between two polypeptides so as to preferentially form a bispecific antibody. The bispecific antibodies can be composed of immunoglobulin chains of the same subclass (*e.g.*, IgG_1 or IgG_3) or different subclasses (*e.g.*, IgG_1 and IgG_3, or IgG_3 and IgG_4).

[00220] Bispecific antibodies can, in some instances contain, IgG_4 and IgG_1, IgG_4 and IgG_2, IgG_4 and IgG_3, or IgG_1 and IgG_3 chain heterodimers. Such heterodimeric heavy chain antibodies can routinely be engineered by, for example, modifying selected amino acids forming the interface of the CH3 domains in human IgG_4 and the IgG_1 or IgG_3, so as to favor heterodimeric heavy chain formation.

[00221] In certain embodiments, an antibody described herein, which binds to the same epitope of PC as an anti-PC antibody described herein, is a human antibody. In certain embodiments, an antibody described herein, which competitively blocks (*e.g.*, in a dose-dependent manner) any one

of the antibodies described herein, from binding to PC, is a human antibody. Human antibodies can be produced using any method known in the art. For example, transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes, can be used. In particular, the human heavy and light chain immunoglobulin gene complexes can be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region can be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes can be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the J_H region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.*, all or a portion of an antigen (*e.g.*, PC). Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM, and IgE antibodies. For an overview of this technology for producing human antibodies, *see* Lonberg N & Huszar D (1995) Int Rev Immunol 13:65-93, herein incorporated by reference in its entirety. For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, *see, e.g.*, International Publication Nos. WO 98/24893, WO 96/34096, and WO 96/33735; and U.S. Patent Nos. 5,413,923, 5,625,126, 5,633,425, 5,569,825, 5,661,016, 5,545,806, 5,814,318, and 5,939,598, all of which are herein incorporated by reference in their entireties. Examples of mice capable of producing human antibodies include the XenoMouse™ (Abgenix, Inc.; U.S. Patent Nos. 6,075,181 and 6,150,184), the HuAb-Mouse™ (Medarex, Inc./Gen Pharm; U.S. Patent Nos. 5,545,806 and 5,569, 825), the TransChromo Mouse™ (Kirin) and the KM Mouse™ (Medarex/Kirin), all of which are herein incorporated by reference in their entireties.

[00222] Human antibodies that specifically bind to PC can be made by a variety of methods known in the art, including the phage display methods described above using antibody libraries derived from human immunoglobulin sequences. *See also*, U.S. Patent Nos. 4,444,887, 4,716,111, and 5,885,793; and International Publication Nos. WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741, all of which are herein incorporated by reference in their entireties.

[00223] In certain embodiments, human antibodies can be produced using mouse-human hybridomas. For example, human peripheral blood lymphocytes transformed with Epstein-Barr virus (EBV) can be fused with mouse myeloma cells to produce mouse-human hybridomas secreting human monoclonal antibodies, and these mouse-human hybridomas can be screened to determine ones which secrete human monoclonal antibodies that specifically bind to a target antigen (*e.g.*, PC). Such methods are known and are described in the art, *see, e.g.*, Shinmoto H *et al.*, (2004) Cytotechnology 46: 19-23; Naganawa Y *et al.*, (2005) Human Antibodies 14: 27-31, each of which is herein incorporated by reference in its entirety.

Kits

[00224] Also provided are kits comprising one or more antibodies described herein, or pharmaceutical compositions or conjugates thereof. In a specific embodiment, provided herein is a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions described herein, such as one or more antibodies provided herein. In certain embodiments, the kits contain a pharmaceutical composition described herein and any prophylactic or therapeutic agent, such as those described herein. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

[00225] Also provided, are kits that can be used in the above methods. In certain embodiments, a kit comprises an antibody described herein, preferably purified antibody, in one or more containers. In a specific embodiment, kits described herein contain a substantially isolated PC antigen as a control. In another specific embodiment, the kits described herein further comprise a control antibody which does not react with PC antigen. In another specific embodiment, kits described herein contain one or more elements for detecting the binding of an antibody to an PC antigen (*e.g.*, the antibody can be conjugated to a detectable substrate such as a fluorescent

compound, an enzymatic substrate, a radioactive compound, or a luminescent compound, or a second antibody which recognizes the first antibody can be conjugated to a detectable substrate). In specific embodiments, a kit provided herein can include a recombinantly produced or chemically synthesized PC antigen. The PC antigen provided in the kit can also be attached to a solid support. In a more specific embodiment, the detecting means of the above-described kit includes a solid support to which an PC antigen is attached. Such a kit can also include a non-attached reporter-labeled anti-human antibody or anti-mouse/rat antibody. In this embodiment, binding of the antibody to the PC antigen can be detected by binding of the said reporter-labeled antibody. In certain embodiments, the present disclosure relates to the use of a kit of the present disclosure for *in vitro* assaying and/or detecting PC antigen in a biological sample.

EXAMPLES

[00226] The following examples are offered by way of illustration and not by way of limitation.

Example 1: Screening summary

[00227] A multi-factor optimization platform was used for antibody optimization. The platform was designed to optimize for affinity, removal of liabilities, thermostability, species cross-reactivity, and selective activation.

[00228] E06 variable heavy (VH) and variable kappa (VK) CDR sequences were grafted onto 4 fully human VH germlines (VH1-46, VH3-15, VH3-23, VH5-51) and 4 fully human VK germlines (VK1-39, VK2-28, VK3-15, VK4-1) respectively. Of the sixteen combinations made, two were selected for platform library construction: E06_VK 1-39 / VH 3-23 and E06_VK 4-1 / VH 3-23. The individual VH and VK sequences are set forth in Table 2.

Table 2: Grafted VH and VK Sequences.

	Sequence (CDR sequences underlined)	SEQ ID NO:
E06_VH3-23	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAP GKGLEWVAASRNKANDYTTEYADSVKGRFTISRDNSKNTL YLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVT VSS	8
E06_VK1-39	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAW YQQKPGKAPKLLIYGASNRYIGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCAQFYSYPLTFGQGTKVEIK	685
E06_VK4-1	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAW	269

	YQQKPGQPPKLLIYGASNRYIGVPDRFSGSGSGTDFTLTISSL QAEDVAVYYCAQFYSYPLTFGGGTKVEIK	

[00229] Phage display libraries of scFv reformatted framework grafts were designed based on structural and sequence analyses to retain CDR residues identified to exhibit key target binding interactions. The remaining CDR residues were used for guided 3-way sequence space exploration to maximize tolerability of human residues while limiting the potential impact on target binding. First, CDRH1, CDRH2, CDRL1, CDRL2, and CDRL3 were modified from parental CDR towards human germline CDRs with up to 4 changes per CDR. Second, CDRH1, CDRH2, CDRL1, CDRL2, and CDRL3 were modified from germline towards parental CDR residues with up to 4 changes. Third, all CDRs were subjected to single amino acid NNK walks omitting residue changes that would generate biochemical liabilities. E06 VK 1-39 / VH 3-23 and VK 4-1 / VH 3-23 scFv libraries were combined, resulting in a total size of 4 x 10^9 transformants (referred to as the "platform library").

[00230] Phosphocholine (PC) conjugated peptides were used for phage panning and scFv primary screening by ELISA. A summary of PC conjugated peptides used is set forth in Table 3.

Table 3: Phosphocholine (PC) Conjugated Peptides Used for Screening.

Peptide #	Conju-gation	Tag	Full Sequence
1	PC	Biotin	Biotin-AGGGGSGGGGSGGGGSAAA-[Tyr(PC)]-acid (SEQ ID NO: 686)
2	PC	-	AGGGGSGGGGSGGGGSAAA-[Tyr(PC)]-acid (SEQ ID NO: 686)
4	-	Biotin	Biotin-AGGGGSGGGGSGGGGSAAA-Tyr-acid (SEQ ID NO: 686)
5	PC	Biotin	Biotin-AEAAAKEAAAKEAAAKEAAAKAAA-[Tyr(PC)]-acid (SEQ ID NO: 687)
6	PC	-	AEAAAKEAAAKEAAAKEAAAKAAA-[Tyr(PC)]-acid (SEQ ID NO: 687)
8	-	Biotin	Biotin-AEAAAKEAAAKEAAAKEAAAKAAA-Tyr-acid (SEQ ID NO: 687)

PC = p-diazophenyl phosphoryl choline

[00231] Phage-peptide complexes were captured on the biotin tag of the peptides with streptavidin coated beads. After washing, bound phage were eluted using triethylamine and titered

to determine enrichment. After each round of panning, eluted phage were used to infected *E. coli* ER2738 for propagation of phage particles to be used in subsequent rounds of selections.

[00232] Single colonies from the Round 4 panning arms (380 colonies from each; 1140 colonies in total) were cultured and scFvs were Sanger sequenced. 736 unique sequences were re-arrayed onto 96-well plates and proceeded to primary screening by scFv ELISA on Peptides 1, 4, 5, and 8.

[00233] A total of 368 unique binders to Peptide 5 and/or Peptide 1 from the primary screen were re-arrayed and proceeded to secondary screening by ELISA (n=2) on Peptides 1, 4, 5, and 8, as well as BSA. A total of 257 unique scFvs were identified with good reproducibility between primary and secondary screening data, and between replicates. These 257 sequences bound specifically to at least one of Peptide 1 and Peptide 5, with no binding to Peptide 4, Peptide 8, or BSA (thresholds for positive OD450 were determined using average OD450 for negative controls (a PD-1 specific scFv) +3x SD: See Example 2 for method).

Example 2: scFv ELISA Summary

[00234] Periplasmic extract (PPE) containing scFv was generated by osmotic shock. Starter cultures (2 x YT with 2% glucose, tetracycline (15 µg/mL) and carbenicillin (100 µg/mL), 700 µl/well in deep well plate) were inoculated with 5-10 µl of glycerol stock and grown over night at 30°C and 700 rpm. The following day, expression cultures (2 x YT with 0.1% glucose and carbenicillin (100 µg/mL), 1 ml/well in deep well plates) were inoculated with 30 ul starter culture and allowed to grow to OD600 0.5 at 37°C and 700 rpm. Cultures were induced with 1 mM IPTG and grown for 6 hours at 25°C and 700 rpm.

[00235] After 6 hours, plates were centrifuged to pellet bacteria and stored overnight at -20°C. The next day, pellets were thawed and resuspended in 80 ul Periplasmic Extraction Buffer with protease inhibitors and put on a shaker for 10 minutes at 4°C and 500 rpm. After 10 minutes, 240 µl water and protease inhibitor were added to each well and incubated for 1 hour at 4°C shaking at 500 rpm. Plates were then centrifuged at 4300 xg for 10 min at 4°C. Supernatants were passed through a filter plate and stored at -80°C.

[00236] For ELISA analysis of scFv binding, 96-well polystyrene plates were coated with Peptide 1, 4, 5, 8 or 100 µL BSA (10 µg/mL) in PBS at 4°C overnight. Plates were washed three times with PBS-Tween and blocked with 100 µL 1% BSA-TBS for 1 hour at room temperature. 96-well streptavidin coated plates were coated with 100 µL biotinylated PC-peptides (1 µg/mL) in PBS for 1 hour at room temperature.

[00237] All plates were washed three times with PBS-Tween before 40 µL aliquots of PPE were added to assay plates along with 50 µL 10% BSA, and plates were incubated for 1 hour at room temperature. After washing, 100 µL HRP conjugated anti-V5 in 5% BSA was added, and plates were incubated at room temperature for 30 mins. Plates were washed and 100µL TMB substrate was added. Color was left to develop at room temperature before the reaction was stopped with 100 µL 1N HCl. The amount of scFv bound to each well was quantitated from absorbance measurement at 450 nm (OD450). Binding data for the 257 unique scFvs identified in Example 1 are summarized in Table 4.

Table 4: scFv ELISA Data.

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB01_A06	1	181	0.74	0.06	1.18	0.06	0.10
PcOxP_DB01_A12	2	182	0.29	0.06	1.04	0.05	0.09
PcOxP_DB01_B01	3	183	0.87	0.07	0.90	0.05	0.10
PcOxP_DB01_B04	4	184	0.57	0.06	1.02	0.05	0.08
PcOxP_DB01_B05	5	185	0.23	0.05	0.74	0.05	0.10
PcOxP_DB01_B07	1	184	1.07	0.06	1.36	0.05	0.11
PcOxP_DB01_B08	6	184	0.41	0.06	0.89	0.05	0.10
PcOxP_DB01_B09	1	186	1.00	0.05	1.42	0.05	0.10
PcOxP_DB01_B11	7	187	1.11	0.05	1.32	0.04	0.09
PcOxP_DB01_C01	8	188	0.71	0.06	1.13	0.05	0.11
PcOxP_DB01_C03	9	189	0.98	0.06	1.37	0.05	0.10
PcOxP_DB01_C04	10	190	1.38	0.05	1.42	0.05	0.08
PcOxP_DB01_C05	4	191	0.79	0.06	1.11	0.06	0.11
PcOxP_DB01_C06	11	192	1.18	0.05	1.31	0.05	0.08
PcOxP_DB01_C08	12	193	0.38	0.06	0.79	0.05	0.10
PcOxP_DB01_C12	13	194	0.88	0.05	1.18	0.05	0.08
PcOxP_DB01_D02	14	195	0.56	0.05	1.27	0.05	0.09
PcOxP_DB01_D05	15	196	0.87	0.06	1.56	0.05	0.10
PcOxP_DB01_D08	16	184	0.58	0.05	1.08	0.05	0.08
PcOxP_DB01_D09	17	197	0.27	0.05	0.66	0.05	0.07
PcOxP_DB01_E04	18	198	0.55	0.05	1.12	0.04	0.07
PcOxP_DB01_E05	1	199	0.95	0.06	1.39	0.06	0.11
PcOxP_DB01_E06	19	200	0.68	0.05	1.05	0.05	0.09
PcOxP_DB01_E11	20	201	0.62	0.05	0.73	0.06	0.09
PcOxP_DB01_F04	21	202	0.36	0.05	0.57	0.05	0.09
PcOxP_DB01_F10	22	203	0.68	0.05	0.98	0.05	0.09
PcOxP_DB01_G01	23	204	0.58	0.06	1.33	0.05	0.09

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB01_G09	24	205	0.92	0.06	1.40	0.05	0.11
PcOxP_DB01_G11	25	184	0.99	0.06	1.32	0.06	0.09
PcOxP_DB01_G12	4	206	0.75	0.07	1.33	0.06	0.09
PcOxP_DB01_H04	26	207	2.01	0.07	1.92	0.07	0.11
PcOxP_DB01_H08	27	208	0.56	0.06	0.85	0.06	0.09
PcOxP_DB01_H10	28	209	0.60	0.06	1.39	0.06	0.08
PcOxP_DB02_A06	9	210	1.12	0.05	1.07	0.05	0.10
PcOxP_DB02_A09	29	211	0.98	0.05	1.30	0.04	0.11
PcOxP_DB02_A10	30	212	0.42	0.05	0.90	0.04	0.11
PcOxP_DB02_A11	31	213	0.64	0.04	0.89	0.04	0.09
PcOxP_DB02_A12	32	214	0.20	0.05	0.27	0.06	0.06
PcOxP_DB02_B02	33	215	0.49	0.05	0.98	0.05	0.11
PcOxP_DB02_B06	34	216	0.35	0.07	0.79	0.04	0.11
PcOxP_DB02_B10	17	217	0.67	0.04	1.03	0.04	0.08
PcOxP_DB02_B12	1	218	2.33	0.05	1.34	0.04	0.10
PcOxP_DB02_C01	35	184	1.03	0.06	1.47	0.05	0.10
PcOxP_DB02_C02	36	184	0.35	0.05	0.62	0.05	0.10
PcOxP_DB02_C06	35	219	0.54	0.05	1.03	0.05	0.11
PcOxP_DB02_C09	35	220	0.69	0.05	1.01	0.04	0.10
PcOxP_DB02_C11	37	184	0.12	0.05	0.24	0.04	0.10
PcOxP_DB02_D01	38	221	0.31	0.05	0.35	0.05	0.09
PcOxP_DB02_D09	39	222	0.16	0.05	0.44	0.04	0.11
PcOxP_DB02_D10	9	223	0.69	0.05	1.01	0.04	0.10
PcOxP_DB02_E01	9	224	0.43	0.05	0.63	0.10	0.11
PcOxP_DB02_E06	40	184	0.06	0.04	0.08	0.04	0.10
PcOxP_DB02_E10	41	225	0.52	0.04	0.79	0.04	0.09
PcOxP_DB02_F02	8	226	0.37	0.05	0.60	0.05	0.11
PcOxP_DB02_F07	42	227	0.43	0.05	0.91	0.05	0.10
PcOxP_DB02_F12	35	228	0.50	0.04	0.81	0.04	0.07
PcOxP_DB02_G06	43	229	0.43	0.06	0.87	0.05	0.08
PcOxP_DB02_G07	4	230	0.52	0.05	0.99	0.09	0.10
PcOxP_DB02_G09	9	231	0.35	0.05	0.71	0.04	0.10
PcOxP_DB02_H03	8	232	0.27	0.05	0.82	0.05	0.08
PcOxP_DB02_H10	1	233	1.43	0.05	1.39	0.05	0.08
PcOxP_DB03_A03	8	234	0.54	0.06	0.81	0.06	0.09
PcOxP_DB03_A08	44	184	0.67	0.06	0.71	0.05	0.11
PcOxP_DB03_A09	1	235	1.02	0.05	1.09	0.05	0.09
PcOxP_DB03_A11	45	236	1.12	0.05	1.08	0.05	0.08
PcOxP_DB03_B02	30	237	2.02	0.05	1.64	0.05	0.07
PcOxP_DB03_C03	46	184	1.36	0.05	1.66	0.05	0.09
PcOxP_DB03_C06	47	238	0.64	0.05	0.61	0.05	0.07
PcOxP_DB03_C11	48	239	1.14	0.05	0.75	0.04	0.07

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB03_C12	1	230	2.74	0.05	1.77	0.05	0.09
PcOxP_DB03_D01	49	190	2.51	0.05	1.60	0.05	0.08
PcOxP_DB03_D07	44	240	0.75	0.06	0.95	0.05	0.12
PcOxP_DB03_D08	50	184	0.54	0.05	0.57	0.05	0.10
PcOxP_DB03_D11	51	241	0.50	0.06	0.66	0.05	0.08
PcOxP_DB03_E01	52	242	2.50	0.06	2.11	0.06	0.09
PcOxP_DB03_E02	53	243	2.00	0.06	1.49	0.05	0.11
PcOxP_DB03_E07	54	184	0.78	0.05	0.86	0.05	0.08
PcOxP_DB03_E08	55	244	0.87	0.05	0.92	0.05	0.09
PcOxP_DB03_E09	56	245	0.39	0.05	0.72	0.05	0.08
PcOxP_DB03_F01	57	246	0.58	0.05	0.80	0.05	0.09
PcOxP_DB03_F10	58	247	0.65	0.05	0.85	0.07	0.09
PcOxP_DB03_G02	59	248	1.33	0.04	1.59	0.05	0.07
PcOxP_DB03_G03	60	249	1.57	0.05	1.80	0.08	0.08
PcOxP_DB03_G06	8	250	2.48	0.06	2.01	0.06	0.10
PcOxP_DB03_G07	61	184	2.18	0.06	1.67	0.05	0.10
PcOxP_DB03_G10	35	251	1.80	0.05	1.21	0.05	0.11
PcOxP_DB03_H03	62	252	0.27	0.07	1.32	0.07	0.12
PcOxP_DB03_H07	1	253	1.91	0.05	1.64	0.05	0.08
PcOxP_DB03_H08	63	254	0.91	0.06	1.18	0.06	0.12
PcOxP_DB03_H09	64	181	0.93	0.06	1.25	0.06	0.11
PcOxP_DB04_A07	65	255	1.54	0.05	2.11	0.05	0.09
PcOxP_DB04_A09	66	256	1.16	0.06	1.96	0.06	0.12
PcOxP_DB04_A10	67	257	0.74	0.06	1.61	0.06	0.11
PcOxP_DB04_A12	68	198	0.71	0.07	1.38	0.06	0.12
PcOxP_DB04_B06	35	258	0.66	0.06	1.06	0.06	0.10
PcOxP_DB04_B08	69	259	1.33	0.06	1.56	0.05	0.11
PcOxP_DB04_C03	70	260	1.34	0.06	1.87	0.06	0.10
PcOxP_DB04_C08	71	261	0.69	0.05	1.07	0.06	0.08
PcOxP_DB04_D08	72	262	1.60	0.07	1.96	0.07	0.12
PcOxP_DB04_F06	73	263	0.75	0.06	1.30	0.06	0.10
PcOxP_DB04_F11	74	264	0.58	0.07	1.27	0.06	0.10
PcOxP_DB04_G06	75	265	1.03	0.07	1.12	0.07	0.11
PcOxP_DB04_H03	76	266	0.80	0.07	1.05	0.08	0.10
PcOxP_DB04_H07	77	267	0.58	0.06	1.02	0.05	0.09
PcOxP_DB04_H08	4	205	0.85	0.07	1.42	0.06	0.09
PcOxP_DB04_H10	78	268	0.54	0.08	1.01	0.07	0.10
PcOxP_DB01_A03	1	269	0.86	0.05	1.38	0.04	0.07
PcOxP_DB01_A04	27	269	0.31	0.04	0.75	0.04	0.07
PcOxP_DB01_A05	79	269	0.83	0.04	1.28	0.04	0.06
PcOxP_DB01_A08	80	270	0.16	0.05	1.12	0.05	0.09
PcOxP_DB01_B02	81	269	0.68	0.06	1.41	0.05	0.09

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB01_B03	22	269	0.82	0.05	1.25	0.05	0.08
PcOxP_DB01_B06	82	269	0.79	0.05	1.45	0.05	0.08
PcOxP_DB01_B10	83	271	0.52	0.05	1.11	0.04	0.08
PcOxP_DB01_B12	84	272	0.56	0.06	1.19	0.05	0.09
PcOxP_DB01_C07	1	273	0.53	0.04	1.10	0.04	0.05
PcOxP_DB01_C09	8	274	0.27	0.05	0.94	0.05	0.07
PcOxP_DB01_C10	8	275	0.13	0.04	0.53	0.04	0.07
PcOxP_DB01_D01	22	276	0.85	0.05	1.12	0.04	0.06
PcOxP_DB01_D04	8	277	0.45	0.08	0.87	0.06	0.07
PcOxP_DB01_D06	85	278	0.41	0.04	0.69	0.04	0.06
PcOxP_DB01_D07	86	279	0.14	0.04	0.60	0.04	0.05
PcOxP_DB01_D10	87	269	0.15	0.05	0.44	0.04	0.06
PcOxP_DB01_D11	88	280	1.37	0.06	2.09	0.05	0.08
PcOxP_DB01_D12	89	269	0.85	0.05	1.48	0.05	0.06
PcOxP_DB01_E01	60	281	0.75	0.05	1.48	0.04	0.05
PcOxP_DB01_E02	90	269	0.46	0.05	1.02	0.05	0.07
PcOxP_DB01_E03	91	282	0.86	0.05	1.54	0.05	0.08
PcOxP_DB01_E07	22	283	0.87	0.05	1.51	0.05	0.07
PcOxP_DB01_E08	92	269	0.47	0.05	0.82	0.04	0.06
PcOxP_DB01_E09	93	284	0.77	0.04	1.26	0.04	0.06
PcOxP_DB01_E10	94	285	0.60	0.07	1.11	0.07	0.11
PcOxP_DB01_F01	95	286	0.60	0.05	1.78	0.05	0.08
PcOxP_DB01_F03	96	269	0.80	0.07	1.41	0.08	0.08
PcOxP_DB01_F06	73	287	0.12	0.04	0.53	0.04	0.07
PcOxP_DB01_F07	97	288	0.31	0.04	0.81	0.04	0.06
PcOxP_DB01_F08	68	289	0.52	0.04	1.22	0.04	0.06
PcOxP_DB01_F11	98	269	1.55	0.07	1.92	0.05	0.07
PcOxP_DB01_F12	99	290	0.76	0.05	1.43	0.05	0.06
PcOxP_DB01_G02	100	291	0.82	0.05	1.20	0.04	0.06
PcOxP_DB01_G03	4	292	0.43	0.05	0.94	0.05	0.07
PcOxP_DB01_G04	4	289	0.56	0.05	1.01	0.07	0.07
PcOxP_DB01_G05	101	284	0.69	0.05	1.24	0.05	0.08
PcOxP_DB01_G06	66	289	0.73	0.05	1.32	0.04	0.06
PcOxP_DB01_G07	89	293	0.46	0.05	1.20	0.04	0.07
PcOxP_DB01_G10	102	294	0.71	0.05	1.52	0.05	0.10
PcOxP_DB01_H01	103	269	0.82	0.07	1.23	0.06	0.09
PcOxP_DB01_H02	22	295	0.74	0.07	1.10	0.06	0.10
PcOxP_DB01_H03	104	296	0.46	0.07	1.29	0.06	0.10
PcOxP_DB01_H06	105	297	0.96	0.05	1.79	0.07	0.11
PcOxP_DB01_H07	106	270	0.10	0.05	0.92	0.05	0.07
PcOxP_DB01_H09	107	269	0.06	0.09	0.09	0.04	0.09
PcOxP_DB02_A04	67	269	0.33	0.04	0.82	0.04	0.09

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB02_A05	62	298	0.99	0.05	1.24	0.04	0.07
PcOxP_DB02_B04	66	269	0.75	0.05	1.32	0.04	0.08
PcOxP_DB02_B07	108	299	0.40	0.04	0.77	0.04	0.06
PcOxP_DB02_B09	109	300	0.27	0.04	0.83	0.04	0.07
PcOxP_DB02_C03	110	301	0.54	0.05	0.61	0.05	0.10
PcOxP_DB02_C04	111	302	0.37	0.05	0.75	0.05	0.08
PcOxP_DB02_C05	112	269	0.64	0.04	0.92	0.04	0.06
PcOxP_DB02_C08	113	303	0.22	0.06	0.39	0.04	0.06
PcOxP_DB02_C10	1	304	0.44	0.04	0.92	0.04	0.06
PcOxP_DB02_C12	72	305	0.97	0.04	1.58	0.04	0.07
PcOxP_DB02_D02	114	306	0.16	0.04	0.27	0.04	0.05
PcOxP_DB02_D03	115	307	0.42	0.04	0.71	0.04	0.08
PcOxP_DB02_E02	116	269	0.09	0.04	0.34	0.05	0.06
PcOxP_DB02_E03	117	308	0.39	0.04	0.75	0.05	0.08
PcOxP_DB02_E08	118	269	0.24	0.04	0.49	0.04	0.07
PcOxP_DB02_E09	110	309	0.56	0.04	0.74	0.04	0.07
PcOxP_DB02_E11	119	310	0.23	0.04	0.76	0.04	0.06
PcOxP_DB02_E12	120	311	0.26	0.05	0.58	0.06	0.06
PcOxP_DB02_F04	121	269	0.47	0.04	0.74	0.05	0.09
PcOxP_DB02_F06	122	312	0.16	0.04	0.45	0.04	0.06
PcOxP_DB02_F09	123	289	0.39	0.04	0.93	0.04	0.08
PcOxP_DB02_F10	9	313	0.51	0.05	1.20	0.04	0.09
PcOxP_DB02_F11	124	314	0.23	0.04	0.66	0.04	0.08
PcOxP_DB02_G02	120	289	1.01	0.04	1.13	0.04	0.06
PcOxP_DB02_G03	125	315	0.06	0.05	0.10	0.05	0.06
PcOxP_DB02_G04	110	316	0.32	0.05	0.70	0.05	0.11
PcOxP_DB02_G05	126	317	1.49	0.05	1.80	0.07	0.11
PcOxP_DB02_H02	127	318	0.07	0.04	0.19	0.06	0.06
PcOxP_DB02_H04	49	319	0.22	0.05	0.20	0.04	0.06
PcOxP_DB02_H05	128	320	0.20	0.04	0.44	0.04	0.09
PcOxP_DB02_H06	9	321	0.92	0.05	1.04	0.05	0.07
PcOxP_DB02_H07	22	322	0.56	0.04	0.88	0.05	0.07
PcOxP_DB02_H08	129	323	0.40	0.04	1.34	0.06	0.07
PcOxP_DB02_H09	130	269	0.25	0.04	0.58	0.04	0.07
PcOxP_DB03_A04	131	324	0.19	0.04	0.47	0.04	0.06
PcOxP_DB03_A05	132	325	0.93	0.04	0.78	0.04	0.06
PcOxP_DB03_A06	133	326	0.99	0.05	1.07	0.05	0.08
PcOxP_DB03_A07	134	327	0.94	0.04	1.01	0.04	0.06
PcOxP_DB03_A10	53	328	0.60	0.04	0.54	0.04	0.06
PcOxP_DB03_A12	135	272	2.28	0.06	1.67	0.05	0.07
PcOxP_DB03_B01	136	329	0.21	0.04	0.64	0.04	0.06
PcOxP_DB03_B03	4	301	1.12	0.04	1.10	0.04	0.07

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB03_B06	137	330	0.68	0.04	1.01	0.05	0.06
PcOxP_DB03_B07	138	269	0.66	0.06	0.81	0.05	0.12
PcOxP_DB03_B08	1	284	2.63	0.05	1.95	0.04	0.07
PcOxP_DB03_B09	22	331	1.09	0.05	0.89	0.05	0.08
PcOxP_DB03_B10	139	269	0.41	0.05	0.71	0.05	0.08
PcOxP_DB03_B11	140	332	0.50	0.05	0.72	0.05	0.07
PcOxP_DB03_B12	141	269	1.21	0.05	0.85	0.05	0.06
PcOxP_DB03_C01	142	333	0.84	0.05	1.47	0.05	0.08
PcOxP_DB03_C04	143	334	2.11	0.04	1.72	0.04	0.07
PcOxP_DB03_C08	144	335	0.98	0.05	0.90	0.05	0.06
PcOxP_DB03_C10	101	298	1.10	0.05	1.10	0.04	0.07
PcOxP_DB03_D02	1	336	0.67	0.05	1.37	0.04	0.09
PcOxP_DB03_D03	145	269	0.73	0.04	1.11	0.04	0.10
PcOxP_DB03_D10	146	337	1.19	0.05	1.41	0.06	0.06
PcOxP_DB03_D12	147	269	0.20	0.04	0.30	0.04	0.06
PcOxP_DB03_E03	17	338	0.27	0.04	0.79	0.04	0.05
PcOxP_DB03_E04	22	320	0.96	0.06	1.20	0.04	0.08
PcOxP_DB03_E11	4	339	1.40	0.05	1.58	0.04	0.07
PcOxP_DB03_E12	148	340	0.57	0.06	0.88	0.06	0.06
PcOxP_DB03_F02	149	341	1.56	0.05	1.68	0.05	0.07
PcOxP_DB03_F03	150	342	1.13	0.05	1.93	0.05	0.08
PcOxP_DB03_F05	151	343	0.73	0.05	1.04	0.04	0.06
PcOxP_DB03_F07	152	344	0.53	0.05	1.19	0.05	0.08
PcOxP_DB03_F09	94	289	0.72	0.05	1.12	0.05	0.08
PcOxP_DB03_F11	153	345	1.47	0.06	1.43	0.06	0.12
PcOxP_DB03_G01	154	346	0.66	0.05	1.19	0.05	0.09
PcOxP_DB03_G09	155	347	0.74	0.05	1.07	0.05	0.07
PcOxP_DB03_G11	22	348	0.26	0.05	0.72	0.05	0.10
PcOxP_DB03_G12	89	282	1.57	0.06	1.91	0.05	0.08
PcOxP_DB03_H02	156	349	1.07	0.05	1.69	0.04	0.05
PcOxP_DB03_H10	157	296	0.24	0.04	0.39	0.07	0.05
PcOxP_DB04_A04	158	350	1.09	0.08	1.90	0.08	0.11
PcOxP_DB04_A05	159	329	0.72	0.04	1.29	0.04	0.06
PcOxP_DB04_A11	24	351	0.64	0.07	1.60	0.08	0.10
PcOxP_DB04_B01	160	352	0.45	0.05	0.78	0.05	0.06
PcOxP_DB04_B07	161	269	0.93	0.06	1.33	0.05	0.09
PcOxP_DB04_B10	162	353	1.05	0.05	1.56	0.04	0.06
PcOxP_DB04_B11	163	269	0.26	0.05	0.31	0.05	0.08
PcOxP_DB04_B12	1	354	0.13	0.04	0.34	0.04	0.09
PcOxP_DB04_C09	164	355	0.55	0.07	1.21	0.06	0.11
PcOxP_DB04_C10	165	269	0.54	0.06	1.03	0.05	0.08
PcOxP_DB04_C11	1	356	0.81	0.05	1.34	0.04	0.07

Binder	SEQ ID NO:		OD450				
	VH	VL	Peptide 1	Peptide 4	Peptide 5	Peptide 8	BSA
PcOxP_DB04_D01	166	357	1.23	0.06	1.66	0.06	0.07
PcOxP_DB04_D05	167	358	0.87	0.05	1.27	0.06	0.08
PcOxP_DB04_D07	110	334	1.02	0.05	1.05	0.05	0.08
PcOxP_DB04_D09	87	359	0.41	0.05	0.83	0.08	0.06
PcOxP_DB04_D10	168	360	1.14	0.05	1.35	0.05	0.07
PcOxP_DB04_D12	169	269	0.64	0.06	1.03	0.05	0.08
PcOxP_DB04_E05	170	269	0.67	0.06	1.03	0.05	0.09
PcOxP_DB04_E06	171	269	1.04	0.04	1.59	0.05	0.07
PcOxP_DB04_E08	172	361	1.39	0.06	2.01	0.05	0.09
PcOxP_DB04_E12	8	362	1.03	0.05	1.39	0.05	0.07
PcOxP_DB04_F01	173	304	0.56	0.07	0.85	0.07	0.09
PcOxP_DB04_F03	174	269	0.58	0.06	0.87	0.05	0.10
PcOxP_DB04_F05	1	363	0.76	0.06	0.97	0.05	0.07
PcOxP_DB04_G01	175	364	0.63	0.07	1.39	0.09	0.09
PcOxP_DB04_G03	176	365	0.19	0.04	0.40	0.05	0.07
PcOxP_DB04_G05	177	269	1.20	0.05	1.67	0.05	0.07
PcOxP_DB04_G08	178	366	1.39	0.05	1.67	0.05	0.07
PcOxP_DB04_G09	179	269	0.48	0.05	1.08	0.06	0.08
PcOxP_DB04_G11	180	367	0.68	0.05	0.79	0.05	0.07
PcOxP_DB04_H01	89	368	1.22	0.06	1.80	0.07	0.07

Example 3: IgG ELISA Summary

[00238] 48 scFv were selected and reformatted along with the parental E06 antibody into human IgG1 using standard techniques. For ELISA analysis of antibody binding, 384-well polystyrene microtitre plates were coated with 20 µL of antigen (PC-BSA at 5µg/mL) in PBS for 2 hours at room temperature. Plates were washed three times with DELFIA® wash buffer, then blocked with 20 µL/well 1% BSA-TBS for 1 hour at room temperature. After washing, 15 µL of the titrated antibody in 1% BSA-TBS was added to wells and incubated for 1 hour at room temperature. After further washing, 15 µL/well of DELFIA® Eu-N1 Anti-Human IgG secondary antibody in TBS was added to wells and incubated for 1 hour at room temperature. Plates were washed again, and the amount of antibody binding to each well was quantitated from TRF measurement following 5 min incubation at room temperature with DELFIA® enhancement buffer. Binding data of the parental E06 IgG1 antibody and various IgG1 binders are summarized in Table 5. No binding to BSA was detected for any of the antibodies shown in Table 5.

[00239] Physical properties (melting temperature, aggregation temperature, and polydispersity index) of the antibodies were determined using an Uncle instrument (Unchained Labs). Physical properties of the parental E06 IgG1 antibody and various IgG1 binders are summarized in Table 5.

Table 5: IgG ELISA Data.

	EC50 (nM)	Physical Properties		
Antibody	PC BSA	Melting Temp. Tm (°C)	Aggregation Temp. Tagg (°C)	Polydispersity Index (PDI)
E06 parental IgG1	0.390	69.5	66.3	0.07
PcOxP_DB01_G05	0.263	71.5	71.65	0.246
PcOxP_DB01_G09	0.308	72.5	73.44	0.058
PcOxP_DB01_H01	0.275	71.58	74.57	0.093
PcOxP_DB03_B11	0.299	71.24	74.52	0.104
PcOxP_DB03_C10	0.285	72	73.29	0.167
PcOxP_DB03_H08	0.445	68.7	69.56	0.182
PcOxP_DB04_A11	0.413	71.5	72.03	0.097
PcOxP_DB04_E05	0.282	70.53	72.22	0.126
PcOxP_DB01_A06	0.43	71.21	72.53	0.197
PcOxP_DB01_B09	0.317	71.5	74.55	0.036
PcOxP_DB01_C04	0.310	33.5	72.81	0.11
PcOxP_DB01_D01	0.274	70.5	70.73	0.029
PcOxP_DB01_D11	0.242	69.14	69.67	0.124
PcOxP_DB01_E05	0.417	71.5	73.26	0.106
PcOxP_DB01_E10	0.316	72.2	74.66	0.172
PcOxP_DB01_F01	0.672	73	72.68	0.347
PcOxP_DB01_G10	0.407	71.5	72.96	0.027
PcOxP_DB01_H02	0.43	72.12	74.88	0.304
PcOxP_DB01_H04	0.456	72	72.97	0.436
PcOxP_DB02_A06	0.643	70	70.54	0.235
PcOxP_DB02_C01	0.64	71.5	72.51	0.207
PcOxP_DB02_H07	0.423	71.74	74.2	0.192
PcOxP_DB03_A09	0.664	70.5	72.92	0.095
PcOxP_DB03_B09	0.426	71	73.2	0.047
PcOxP_DB03_C03	0.339	70.22	73.18	0.231
PcOxP_DB03_C12	0.436	70	73.79	0.098
PcOxP_DB03_D08	0.401	70.23	71.27	0.149
PcOxP_DB03_E01	0.857	72.01	73.07	0.166
PcOxP_DB03_G07	0.636	73.06	74.2	0.223
PcOxP_DB03_G12	0.557	72.74	73.67	0.06
PcOxP_DB04_A09	0.269	72.5	72.15	0.023
PcOxP_DB04_E08	0.251	72.73	76.24	0.167

Antibody	EC50 (nM)	Physical Properties		
	PC BSA	Melting Temp. Tm (°C)	Aggregation Temp. Tagg (°C)	Polydispersity Index (PDI)
PcOxP_DB01_F06	0.216	72.18	71.28	0.219
PcOxP_DB02_F10	0.659	72	73.59	0.12
PcOxP_DB02_G04	0.231	70	67.12	0.143
PcOxP_DB04_G01	0.257	72.5	74.34	0.288
PcOxP_DB01_B06	0.219	72.6	74.28	0.437
PcOxP_DB01_F04	0.344	71	70.95	0.184
PcOxP_DB01_F11	0.244	71.18	76.16	0.074
PcOxP_DB01_H08	0.244	70.51	70.08	0.092
PcOxP_DB02_A05	0.264	71.5	73.63	0.25
PcOxP_DB02_B04	0.278	71.58	76.93	0.078
PcOxP_DB03_F09	0.28	72.62	73.62	0.129
PcOxP_DB03_G03	0.216	58.52	73.65	0.22
PcOxP_DB03_G11	0.244	73.06	74.11	0.217
PcOxP_DB03_H03	0.229	70.5	70.1	0.156
PcOxP_DB04_A04	0.294	74	76.96	0.134
PcOxP_DB02_C09	0.394	72	68.48	0.265

Example 4: Further IgG Characterization

[00240] Select human IgG1 antibodies (see Example 3) were further analyzed for antibody yield, stress testing, and immunogenicity characteristics. Yield was determined by transfection of HEK293 cells and subsequent expression in 25 mL cultures. For several of the antibodies, yield was determined in a scaled-up 40 L transient transfection culture. Antibody products were purified using protein A, and the resulting amount of antibody was measured via absorbance at 280 nm (OD280). The yield values for the parental E06 IgG1 antibody and select IgG1 binders are shown in Table 6.

Table 6: Yield Data.

Antibody	Yield – 25 mL culture (mg)	Yield – 40 L culture (mg/L)
E06 parental IgG1	--	15
PcOxP_DB01_H08	3.3	649
PcOxP_DB03_C03	3.4	392
PcOxP_DB01_F11	8.5	
PcOxP_DB01_B09	5.2	
PcOxP_DB01_G09	4.8	
PcOxP_DB03_C12	3.1	

PcOxP_DB01_E05	5.1	

[00241] The parental E06 IgG1 antibody and the human IgG1 PcOxP_DB01_H08 antibody were analyzed in forced degradation studies to compare the relative stability and resistance to stress between the antibodies. Samples of each antibody were subjected to temperature stress, oxidation stress, and low and high pH stress, and the samples were analyzed and compared to non-stressed samples. Various analytical techniques were used to analyze the samples. In addition to concentration measurement and visual inspection, chemical stability was assessed via protein level RPC-MS at the intact and reduced antibody level, peptide mapping analysis under reducing conditions, iCIEF analysis, and CGE-SDS in non-reducing and reducing conditions, and physical stability was assessed using SE-HPLC.

[00242] For temperature stress, samples of each antibody were stored at 40°C for 2 weeks, 3 weeks, or 4 weeks. For low pH stress, the pH in samples of each antibody was adjusted to 3.2 using 0.12M HCl, and the samples were incubated at 25°C for 2 hours prior to buffer exchange back to formulation buffer. For high pH stress (forced deamidation), the pH in samples of each antibody was adjusted to 9.0 using 0.5 M Tris pH 11, and the samples were incubated for 3 days at 37°C prior to buffer exchange back to formulation buffer. For oxidative stress, 3% H2O2 solution was added to samples of each antibody to reach a final concentration of 0.03%, and the samples were incubated for 1 day at 25°C prior to buffer exchange back to formulation buffer. The stress testing and stability assay results are summarized qualitatively in Table 7 ("+": moderately stable; "++": highly stable).

Table 7: Stress Testing and Stability Comparison.

Antibody	Storage at 40°C	Low pH stress	Forced deamidation	Oxidative stress
E06 parental IgG1	+	++	+	++
PcOxP_DB01_H08	++	++	++	++

[00243] *In vivo* immunogenicity for the parental E06 IgG1 antibody and the human IgG1 PcOxP_DB01_H08 and PcOxP_DB03_C03 antibodies was predicted using the *in vitro* Epibase® immunogenicity assay (Lonza Biologics), the *in silico* Epibase® platform (Lonza Biologics) and the *in silico* ISPRI™ platform (EpiVax, Inc.). The immunogenicity profiles are summarized in Table 8. Overall, the immunogenicity assays show that PcOxP_DB01_H08 and

PcOxP_DB03_C03 each have a low immunogenicity risk and a favorable profile when compared with several established antibody drugs.

Table 8: Immunogenicity Assay Data.

Antibody	*In vitro* Epibase® (% responders)*	*In silico* Epibase® score	*In silico* ISPRI™ score**
E06 parental IgG1	17	2203	+7.44
PcOxP_DB01_H08	16	906	-50.09
PcOxP_DB03_C03	22	1048	--

*: 32 donor samples, KLH positive control shows 100% effect
**: a score of 0 indicates predicted immunogenic responses in approximately 5% of patients

SEQUENCE LISTING

SEQ ID NO	SEQUENCE
1	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
2	EVQLLESGGGLVQPGGSLRLSCAASGFGFSDFYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYYDVWGQGTLVTVSS
3	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYIEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYLGSSYWYFDVWGQGTLVTVSS
4	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
5	EVQLLESGGGLVQPGGSLRLSCAASGFTASDFYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
6	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDSYMEWVRQAPGKGLEWVAASRNKANDYTTSY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
7	EVQLLESGGGLVQPGGSLRLSCAASGFTFEDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYFGSSYWYFDVWGQGTLVTVSS
8	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
9	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
10	EVQLLESGGGLVQPGGSLRLSCAASGFQFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
11	EVQLLESGGGLVQPGGSLRLSCAASGFEFSDNYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
12	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYASSYWYFDVWGQGTLVTVSS
13	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEL ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
14	EVQLLESGGGLVQPGGSLRLSCAASGFEFSDFYMEWVRQAPGKGLEWVAASRGKGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS

15	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSPYWYFDVWGQGTLVTVSS
16	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDSWGQGTLVTVSS
17	EVQLLESGGGLVQPGGSLRLSCAASGFTESDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
18	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDTWGQGTLVTVSS
19	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDLWGQGTLVTVSS
20	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYVTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
21	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
22	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
23	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRNKGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
24	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANTYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
25	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKNNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYFGSSYWYFDVWGQGTLVTVSS
26	EVQLLESGGGLVQPGGSLRLSCAASGFAFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSHYWYFDVWGQGTLVTVSS
27	EVQLLESGGGLVQPGGSLRLSCAASGFTHSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
28	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKNNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
29	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDTYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
30	EVQLLESGGGLVQPGGSLRLSCAASGFAFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
31	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNIANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
32	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDDYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYQGSSYWYFDVWGQGTLVTVSS
33	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNSGNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
34	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDNYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
35	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
36	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTVEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGHSYWYFDVWGQGTLVTVSS
37	EVQLLESGGGLVQPGGSLRLSCAASGFTSSDFYMEWVRQAPGKGLEWVAASRNKANDYYTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
38	EVQLLESGGGLVQPGGSLRLSCAASGFGFSDFYMEWVRQAPGKGLEWVAASRHKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
39	EVQLLESGGGLVQPGGSLRLSCAASGFTFSTFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS

40	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDEYMEWVRQAPGKGLEWVAASRGKGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
41	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYMEWVRQAPGKGLEWVAASRNKANDYQTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
42	EVQLLESGGGLVQPGGSLRLSCAASGFWFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
43	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNQANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSPYWYFDVWGQGTLVTVSS
44	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDVYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
45	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNQANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYLDVWGQGTLVTVSS
46	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
47	EVQLLESGGGLVQPGGSLRLSCAASGATFSDFYMEWVRQAPGKGLEWVAASRNGANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGNSYWYFDVWGQGTLVTVSS
48	EVQLLESGGGLVQPGGSLRLSCAASGFDFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTDY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYFGSSYWYFDVWGQGTLVTVSS
49	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDEYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
50	EVQLLESGGGLVQPGGSLRLSCAASGFWFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSAYWYFDVWGQGTLVTVSS
51	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGHSYWYFDVWGQGTLVTVSS
52	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANDYTVEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
53	EVQLLESGGGLVQPGGSLRLSCAASGWTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
54	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDNYMEWVRQAPGKGLEWVAASRNKANDYTNEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
55	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSFYMEWVRQAPGKGLEWVAASRNAANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDLWGQGTLVTVSS
56	EVQLLESGGGLVQPGGSLRLSCAASGFTASDFYMEWVRQAPGKGLEWVAASRNKANDQTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDSWGQGTLVTVSS
57	EVQLLESGGGLVQPGGSLRLSCAASGFTFNDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
58	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRNSGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
59	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYIEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
60	EVQLLESGGGLVQPGGSLRLSCAASGFTSSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
61	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGQSYWYFDVWGQGTLVTVSS
62	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
63	EVQLLESGGGLVQPGGSLRLSCAASGGTFSDFYMEWVRQAPGKGLEWVAASRNKANTYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
64	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDAYMEWVRQAPGKGLEWVAASRNKANSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS

65	EVQLLESGGGLVQPGGSLRLSCAASGFTQSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
66	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
67	EVQLLESGGGLVQPGGSLRLSCAASGDTFSDFYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
68	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDGYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
69	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDDYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
70	EVQLLESGGGLVQPGGSLRLSCAASGFTTSDFYMEWVRQAPGKGLEWVAASRNKANSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
71	EVQLLESGGGLVQPGGSLRLSCAASGETFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
72	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
73	EVQLLESGGGLVQPGGSLRLSCAASGDTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
74	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRGKGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSTWYFDVWGQGTLVTVSS
75	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRWKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYESSYWYFDVWGQGTLVTVSS
76	EVQLLESGGGLVQPGGSLRLSCAASGFPFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
77	EVQLLESGGGLVQPGGSLRLSCAASGFTFEDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
78	EVQLLESGGGLVQPGGSLRLSCAASGATFSDFYVEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
79	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGNSYWYFDVWGQGTLVTVSS
80	EVQLLESGGGLVQPGGSLRLSCAASGFTQSDFYMEWVRQAPGKGLEWVAAIRNKANSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
81	EVQLLESGGGLVQPGGSLRLSCAASGGTFSDFYMEWVRQAPGKGLEWVAASRNKANSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
82	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSTWYFDVWGQGTLVTVSS
83	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTTY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSHWYFDVWGQGTLVTVSS
84	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKGNSYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
85	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDSWGQGTLVTVSS
86	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGDSYWYFDVWGQGTLVTVSS
87	EVQLLESGGGLVQPGGSLRLSCAASGFTDSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
88	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYNDVWGQGTLVTVSS
89	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS

90	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKGNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
91	EVQLLESGGGLVQPGGSLRLSCAASGFGFSDFYMEWVRQAPGKGLEWVGASRNKHNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
92	EVQLLESGGGLVQPGGSLRLSCAASGDTFSDFYMEWVRQAPGKGLEWVAASRNKANAYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGQSYWYFDVWGQGTLVTVSS
93	EVQLLESGGGLVQPGGSLRLSCAASGNTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
94	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKFNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
95	EVQLLESGGGLVQPGGSLRLSCAASGFPFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSPYWYFDVWGQGTLVTVSS
96	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDSYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
97	EVQLLESGGGLVQPGGSLRLSCAASGDTFSDFYLEWVRQAPGKGLEWVAASRNKANGYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYHSSYWYFDVWGQGTLVTVSS
98	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYYDVWGQGTLVTVSS
99	EVQLLESGGGLVQPGGSLRLSCAASGFTHSDFYMEWVRQAPGKGLEWVAASRNKANGYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDSWGQGTLVTVSS
100	EVQLLESGGGLVQPGGSLRLSCAASGFLFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTTY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSHYWYFDVWGQGTLVTVSS
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102	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKNNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
103	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYYMEWVRQAPGKGLEWVAASRNKANLYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSTWYFDVWGQGTLVTVSS
104	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRGKGNSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
105	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKGNSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
106	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDIYGSSYWYFDVWGQGTLVTVSS
107	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKANTYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYDDVWGQGTLVTVSS
108	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYMEWVRQAPGKGLEWVAASRNNANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
109	EVQLLESGGGLVQPGGSLRLSCAASGFTNSDFYMEWVRQAPGKGLEWVAASRNKFNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
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111	EVQLLESGGGLVQPGGSLRLSCAASGQTFSDFYMEWVRQAPGKGLEWVAASRNKANGYTTEY TDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
112	EVQLLESGGGLVQPGGSLRLSCAASGFTASDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
113	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDPYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSPYWYFDVWGQGTLVTVSS
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115	EVQLLESGGGLVQPGGSLRLSCAASGFTQSDFYMEWVRQAPGKGLEWVAASRNKANAYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGYSYWYFDVWGQGTLVTVSS
116	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDEYMEWVRQAPGKGLEWVAASRNSGNSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
117	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRWKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSQWYFDVWGQGTLVTVSS
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119	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDQYMEWVRQAPGKGLEWVAASRNKANDYTVEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
120	EVQLLESGGGLVQPGGSLRLSCAASGFGFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
121	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRNSGNSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYFGSSYWYFDVWGQGTLVTVSS
122	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDEYMEWVRQAPGKGLEWVAASRNKANDFTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDFYGSSYWYFDVWGQGTLVTVSS
123	EVQLLESGGGLVQPGGSLRLSCAASGFQFSDFYMEWVRQAPGKGLEWVAASRNKGNSYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
124	EVQLLESGGGLVQPGGSLRLSCAASGTTFSDFYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
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137	EVQLLESGGGLVQPGGSLRLSCAASGITFSDFYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
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143	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYNDVWGQGTLVTVSS
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156	EVQLLESGGGLVQPGGSLRLSCAASGFTESDFYMEWVRQAPGKGLEWVAASRNKYNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
157	EVQLLESGGGLVQPGGSLRLSCAASGFTFDDFYMEWVRQAPGKGLEWVAASRNEANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
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166	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKGNDYTTAY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
167	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNVANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
168	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRWKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
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171	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSPYWYFDVWGQGTLVTVSS
172	EVQLLESGGGLVQPGGSLRLSCAASGFTSSDFYLEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
173	EVQLLESGGGLVQPGGSLRLSCAASGFTFSPFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
174	EVQLLESGGGLVQPGGSLRLSCAASGFTASDFYMEWVRQAPGKGLEWVAASRWKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDIYGSSYWYFDVWGQGTLVTVSS
175	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYLSSYWYFDVWGQGTLVTVSS
176	EVQLLESGGGLVQPGGSLRLSCAASGFTTSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDYWGQGTLVTVSS
177	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDFYGSSYWYFDVWGQGTLVTVSS
178	EVQLLESGGGLVQPGGSLRLSCAASGFTGSDFYMEWVRQAPGKGLEWVAASRNKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
179	EVQLLESGGGLVQPGGSLRLSCAASGNTFSDFYMEWVRQAPGKGLEWVAASRNKWNDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
180	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMEWVRQAPGKGLEWVAASRWKANDYTTEY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDYYGSSYWYFDVWGQGTLVTVSS
181	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAEFYSYPLTFGGGTKVEIK
182	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNREI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFYSYPLTFGGGTKVEIK
183	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASHRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYAYPLTFGGGTKVEIK
184	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
185	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASSLQI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
186	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYT GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYHYPLTFGGGTKVEIK
187	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYH GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
188	DIQMTQSPSSLSASVGDRVTITCVASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
189	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYQYPLTFGGGTKVEIK

190	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
191	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGSSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYAYPLTFGGGTKVEIK
192	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRFI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
193	DIQMTQSPSSLSASVGDRVTITCRASESISSSKNKVHYLAWYQQKPGKAPKLLIYGASNRYY GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
194	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGAANRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYVYPLTFGGGTKVEIK
195	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCGQFYSYPLTFGGGTKVEIK
196	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYV GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
197	DIQMTQSPSSLSASVGDRVTITCTASESLYSAKHKVHYLAWYQQKPGKAPKLLIYGSSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYDYPLTFGGGTKVEIK
198	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYD GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
199	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVNYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYQYPLTFGGGTKVEIK
200	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYVAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
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202	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGAVNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYRYPLTFGGGTKVEIK
203	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNGYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYTYPLTFGGGTKVEIK
204	DIQMTQSPSSLSASVGDRVTITCTASESLYGSKHKVHYLAWYQQKPGKAPKLLIYGASNRYS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
205	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNLYS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
206	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYF GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
207	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
208	DIQMTQSPSSLSASVGDRVTITCRASESISSSKHKHYLAWYQQKPGKAPKLLIYGASNRYIG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYVYPLTFGGGTKVEIK
209	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYF GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYQYPLTFGGGTKVEIK
210	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGLSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
211	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYWYPLTFGGGTKVEIK
212	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYAYPLTFGGGTKVEIK
213	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYH GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
214	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGAFNRYT GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYTYPLTFGGGTKVEIK

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216	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCTQFYSYPLTFGGGTKVEIK
217	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYVYPLTFGGGTKVEIK
218	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGQSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
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224	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASGRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
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226	DIQMTQSPSSLSASVGDRVTITCFASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRGI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
227	DIQMTQSPSSLSASVGDRVTITCTASQSLYSSKNKVHYLAWYQQKPGKAPKLLIYGESNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
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237	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYD GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYEYPLTFGGGTKVEIK
238	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYVYPLTFGGGTKVEIK
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242	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGTSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYEYPLTFGGGTKVEIK
243	DIQMTQSPSSLSASVGDRVTITCTASESLYSQKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYYYPLTFGGGTKVEIK
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246	DIQMTQSPSSLSASVGDRVTITCEASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRLI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYEYPLTFGGGTKVEIK
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248	DIQMTQSPSSLSASVGDRVTITCTASEELYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
249	DIQMTQSPSSLSASVGDRVTITCTASQSISSSKHKVHYLAWYQQKPGKAPKLLIYGASNHYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
250	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYEYPLTFGGGTKVEIK
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252	DIQMTQSPSSLSASVGDRVTITCTASESLSSSKHKHYLAWYQQKPGKAPKLLIYGASSRYSG VPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
253	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRDI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCGQFYSYPLTFGGGTKVEIK
254	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGSSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYQYPLTFGGGTKVEIK
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261	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHGVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYQYPLTFGGGTKVEIK
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264	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYA GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCGQFYSYPLTFGGGTKVEIK

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268	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGPSNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGGGTKVEIK
269	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
270	DIVMTQSPDSLAVSLGERATINCTASESVYSSKNKKHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
271	DIVMTQSPDSLAVSLGERATINCTASESLYSSKGKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCVQFYSYPLTFGGGTKVEIK
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273	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYD GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
274	DIVMTQSPDSLAVSLGERATINCTASQSVYSSKNKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
275	DIVMTQSPDSLAVSLGERATINCTSSQSLLSSSHNKNYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
276	DIVMTQSPDSLAVSLGERATINCTASESLYSPKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYIYPLTFGGGTKVEIK
277	DIVMTQSPDSLAVSLGERATINCTASESLWSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
278	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYIYPLTFGGGTKVEIK
279	DIVMTQSPDSLAVSLGERATINCKASQSVLSSKNNVNYLAWYQQKPGQPPKLLIYGASNRYS GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
280	DIVMTQSPDSLAVSLGERATINCTASESLYSSKWKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
281	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRVI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCANFYSYPLTFGGGTKVEIK
282	DIVMTQSPDSLAVSLGERATINCKSSESVYSSKHKKHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
283	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVDYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
284	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCANFYSYPLTFGGGTKVEIK
285	DIVMTQSPDSLAVSLGERATINCTASESLYSPKHKVHYLAWYQQKPGQPPKLLIYGAFNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK
286	DIVMTQSPDSLAVSLGERATINCTASESVYSSKNKKHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYTYPLTFGGGTKVEIK
287	DIVMTQSPDSLAVSLGERATINCKSSQSLYYSSNKKNYLAWYQQKPGQPPKLLIYGASNRYG GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYRYPLTFGGGTKVEIK
288	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYI GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAHFYSYPLTFGGGTKVEIK
289	DIVMTQSPDSLAVSLGERATINCTASESLYSSKHKVHYLAWYQQKPGQPPKLLIYGASNRYS GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCAQFYSYPLTFGGGTKVEIK

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370	FGFSDFYME
371	FTFSDQYIE
372	FTFSDGYME
373	FTASDFYME
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383	FTFSSYYME
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420	ITFSDFYME
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423	FSFSDFYME
424	FTFDDFYME
425	FTFSDFYIE
426	FTSSDFYLE
427	FTFSPFYME
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429	AASRNKWNDYTTEYA
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431	AASRNKANDYTTELA
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433	AASRNKANDYVTEYA
434	AASRNKYNDYTTEYA
435	AASRNKGNSYTTEYA
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442	AASRHKANDYTTEYA
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483	AASRNKANYYTTEYA
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492	CARDYYGSSYWYFDLW
493	CARDYYGSHYWYFDVW
494	CARDYQGSSYWYFDVW
495	CARDYYGHSYWYFDVW
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497	CARDYYGNSYWYFDVW
498	CARDYYGSAYWYFDVW
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504	CARDYYGSSYWYNDVW
505	CARDYYHSSYWYFDVW
506	CARDIYGSSYWYFDVW
507	CARDYYGSSYWYDDVW
508	CARDYYGYSYWYFDVW
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511	CARDYYGSSYWYHDVW
512	CARDYYGSSYWYFDPW
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516	CARDYYFSSYWYFDVW
517	CARDYYDSSYWYFDVW
518	CARDYYGASYWYFDVW
519	CARDHYGSSYWYFDVW
520	CARDYYGESYWYFDVW
521	CARDYYLSSYWYFDVW
522	CARDYYGSSYWYFDYW
523	TASESLYSSKHKVHYLA
524	VASESLYSSKHKVHYLA
525	RASESISSSKNKVHYLA
526	TASESLYSAKHKVHYLA

527	TASESLYSSKHKVNYLA
528	TASESLYSSKHKVHYVA
529	TASFSLYSSKHKVHYLA
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531	RASESISSSKHKHYLA
532	TASEWLYSSKHKVHYLA
533	TATESLYSSKHKVHYLA
534	TASESLYSGKHKVHYLA
535	FASESLYSSKHKVHYLA
536	TASQSLYSSKNKVHYLA
537	EASESLYSSKHKVHYLA
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539	TASESLYSQKHKVHYLA
540	TASESLYSSKHSVHYLA
541	TASEELYSSKHKVHYLA
542	TASQSISSSKHKVHYLA
543	TASESLSSSKHKHYLA
544	TAEESLYSSKHKVHYLA
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546	TASESLSSSKHKVHYLA
547	TASQSLYSSKHKVHYLA
548	RASESLYSSLHKYLA
549	TASESVYSSKNKKHYLA
550	TASESLYSSKGKVHYLA
551	TASQSVYSSKNKVHYLA
552	TSSQSLLSSSHNKNYLA
553	TASESLYSPKHKVHYLA
554	TASESLWSSKHKVHYLA
555	KASQSVLSSKNNVNYLA
556	TASESLYSSKWKVHYLA
557	KSSESVYSSKHKKHYLA
558	TASESLYSSKHKVDYLA
559	KSSQSLYYSSNKKNYLA
560	TASTSLYSSKHKVHYLA
561	KASQSLYSSKHKKHYLA
562	TASSSLYSSKHKVHYLA
563	TASESLYSVKHKVHYLA
564	GASESLYSSKSKVHYLA
565	TSSESVYSSSHKVHYLA
566	TASESLYSSKHKKNYLA
567	KSSESLLYSKNNKNYLA

568	TASESIYSSKHKVHYLA
569	TSSQSVLSSKHNKNYLA
570	TASEDLYSSKHKVHYLA
571	KASQSVLYSKNKKHYLA
572	TASESLYSSKHKLHYLA
573	TASESLYSSKHKVVYLA
574	TSSESLYSSKNKVNYLA
575	TSSQSLYSSKHNKHYLA
576	TASESLYSNKHKVHYLA
577	TASENLYSSKHKVHYLA
578	TASESLYSSKIKVHYLA
579	KSSQSLLYSKNNVNYLA
580	KSSESLYSSKNKVHYLA
581	TSSESLLSSKHKVHYLA
582	TASQSVYSSKHKKHYLA
583	TASQSVYSSKHNKHYLA
584	TSSQSLLYSSNKKHYLA
585	KSSQSVLSSKHKKNYLA
586	TASQSVYSSKNKKHYLA
587	TASESVLSSKHKKNYLA
588	TASVSLYSSKHKVHYLA
589	TASESLYSTKHKVHYLA
590	TASESLYSSNHKVHYLA
591	GASNRYI
592	GASNREI
593	GASHRYI
594	GASSLQI
595	GASNRYT
596	GASNRYH
597	GSSNRYI
598	GASNRFI
599	GASNRYY
600	GAANRYI
601	GASNRYV
602	GASNRYD
603	GASNRYP
604	GAVNRYI
605	GASNGYI
606	GASNRYS
607	GASNLYS
608	GASNRYF

609	GASNLQS
610	GLSNRYI
611	GASNRQS
612	GAFNRYT
613	GASNRLI
614	GQSNRYI
615	GASNRNI
616	GAGNRYI
617	GASNRYG
618	GASGRYI
619	GASNLQI
620	GASNRGI
621	GESNRYI
622	GVSNRYI
623	GASNRPI
624	GASFRYI
625	GADNRYI
626	GASNRYQ
627	GASSRYI
628	GTSNRYI
629	GASNHYI
630	GASNRQI
631	GASSRYS
632	GASNRDI
633	GISNRYI
634	GASSLYS
635	GASNRAI
636	GASNRYA
637	GASNRVI
638	GPSNRYI
639	GAFNRYI
640	GANNRYI
641	GAHNRYI
642	GNSNRYI
643	GASWRYI
644	GASTRYS
645	GASNRYW
646	GASNRYL
647	GASNRYN
648	GASQRYI
649	GAQNRYI

650	GATNRYI
651	GASNPYI
652	GASTRYI
653	GAENRYI
654	GASHRQI
655	GASNTYI
656	CAEFYSYPLTF
657	CQQFYSYPLTF
658	CAQFYAYPLTF
659	CAQFYSYPLTF
660	CAQFYHYPLTF
661	CAQFYQYPLTF
662	CAQFYYYPLTF
663	CAQFYVYPLTF
664	CGQFYSYPLTF
665	CAQFYDYPLTF
666	CAQFYRYPLTF
667	CAQFYTYPLTF
668	CAQFYWYPLTF
669	CTQFYSYPLTF
670	CAQFYFYPLTF
671	CAQFYEYPLTF
672	CAHFYSYPLTF
673	CAQFYKYPLTF
674	CAQFFSYPLTF
675	CVQFYSYPLTF
676	CAQFYIYPLTF
677	CANFYSYPLTF
678	CAQYYSYPLTF
679	CAQFYLYPLTF
680	CAQFYNYPLTF
681	CASFYSYPLTF
682	CAAFYSYPLTF
683	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPG
684	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCL

	VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHE ALHNHYTQKSLSLSLG
685	DIQMTQSPSSLSASVGDRVTITCTASESLYSSKHKVHYLAWYQQKPGKAPKLLIYGASNRYI GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQFYSYPLTFGQGTKVEIK
686	AGGGGSGGGGSGGGGSAAA (Note: peptide can be conjugated with biotin at the N terminus residue, PC linked Tyr at the C terminus residue)
687	AEAAAKEAAAKEAAAKEAAAKAAA (Note: peptide can be conjugated with biotin at the N terminus residue, PC linked Tyr at the C terminus residue
688	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
689	GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPSKQS NNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
690	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQS NNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
691	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQS NNKYAASSYLSLTPEQWKSHKSYSCQVTHEGSTVEKTVAPTECS
692	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVKVAWKADGSPVNTGVETTTPSKQS NNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPAECS
693	GQPKAAPSVTLFPPSSEELQANKATLVCLVSDFNPGAVTVAWKADGSPVKVGVETTKPSKQS NNKYAASSYLSLTPEQWKSHRSYSCRVTHEGSTVEKTVAPAECS

* * *

[00244] The invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims.

[00245] All references (*e.g.*, publications or patents or patent applications) cited herein are incorporated herein by reference in their entireties and for all purposes to the same extent as if each individual reference (*e.g.*, publication or patent or patent application) was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

[00246] Other embodiments are within the following claims.

WHAT IS CLAIMED:

1. An antibody that specifically binds phosphocholine (PC), the antibody comprising: a VH comprising the CDRH1, CDRH2, and CDRH3 amino acid sequences of any one of the VH amino acid sequences set forth in SEQ ID NOs: 1-180; and a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences of any one of the VL amino acid sequences set forth in SEQ ID NOs: 181-368.

2. The antibody of claim 1, wherein the antibody comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences of the VH and VL amino acid sequences, respectively, set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311;

121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331; 139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368.

3. The antibody of claim 1 or 2, wherein the antibody comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383,

434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

4. The antibody of any one of the preceding claims, wherein the antibody comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523,

591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

5. The antibody of any one of the preceding claims, wherein the antibody comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences, set forth in SEQ

ID NOs: 369, 428, 484, 523, 591, and 656; 370, 429, 485, 523, 592, and 657; 371, 428, 486, 523, 593, and 658; 372, 428, 484, 523, 591, and 659; 373, 429, 484, 523, 594, and 659; 369, 428, 484, 523, 591, and 659; 374, 430, 484, 523, 591, and 659; 369, 428, 484, 523, 595, and 660; 375, 428, 487, 523, 596, and 659; 376, 428, 484, 524, 591, and 659; 377, 428, 484, 523, 591, and 661; 378, 428, 484, 523, 591, and 662; 372, 428, 484, 523, 597, and 658; 379, 428, 484, 523, 598, and 662; 372, 428, 488, 525, 599, and 659; 376, 431, 484, 523, 600, and 663; 380, 432, 484, 523, 591, and 664; 372, 428, 489, 523, 601, and 659; 381, 428, 490, 523, 591, and 659; 382, 428, 484, 526, 597, and 665; 381, 428, 491, 523, 602, and 659; 369, 428, 484, 527, 591, and 661; 377, 428, 492, 528, 591, and 662; 376, 433, 484, 529, 603, and 662; 383, 434, 484, 523, 604, and 666; 383, 428, 484, 523, 605, and 667; 384, 435, 484, 530, 606, and 659; 369, 436, 484, 523, 607, and 659; 372, 437, 487, 523, 591, and 659; 372, 428, 484, 523, 608, and 659; 385, 428, 493, 523, 609, and 662; 386, 428, 484, 531, 591, and 663; 372, 437, 484, 523, 608, and 661; 377, 428, 484, 523, 610, and 659; 387, 428, 484, 523, 611, and 668; 385, 428, 484, 523, 611, and 658; 372, 438, 484, 523, 596, and 662; 388, 428, 494, 523, 612, and 667; 369, 439, 484, 523, 613, and 668; 389, 428, 484, 523, 591, and 669; 382, 428, 484, 523, 591, and 663; 369, 428, 484, 523, 614, and 659; 381, 428, 484, 523, 591, and 659; 376, 440, 495, 523, 591, and 659; 381, 428, 484, 532, 615, and 662; 381, 428, 484, 523, 616, and 670; 390, 441, 484, 523, 591, and 659; 370, 442, 484, 523, 591, and 668; 391, 428, 484, 523, 617, and 671; 377, 428, 484, 533, 595, and 659; 377, 428, 484, 523, 618, and 659; 392, 432, 484, 523, 591, and 659; 377, 443, 484, 534, 619, and 662; 376, 428, 484, 535, 620, and 659; 393, 428, 484, 536, 621, and 659; 381, 428, 484, 537, 603, and 671; 383, 444, 489, 523, 622, and 59; 372, 428, 484, 523, 617, and 659; 377, 428, 484, 523, 623, and 659; 376, 428, 484, 538, 607, and 672; 369, 428, 484, 523, 616, and 671; 376, 428, 484, 523, 624, and 659; 394, 428, 484, 523, 591, and 659; 369, 428, 484, 523, 620, and 659; 383, 444, 496, 523, 625, and 660; 385, 428, 484, 523, 602, and 671; 376, 434, 484, 523, 591, and 659; 395, 445, 497, 523, 611, and 663; 396, 446, 487, 523, 626, and 670; 369, 428, 484, 523, 617, and 659; 392, 428, 484, 523, 591, and 662; 394, 428, 484, 523, 606, and 673; 393, 428, 498, 523, 591, and 659; 376, 428, 495, 523, 627, and 671; 369, 440, 484, 523, 628, and 671; 397, 428, 484, 539, 591, and 662; 389, 447, 484, 523, 591, and 659; 398, 448, 492, 523, 591, and 670; 373, 449, 490, 523, 611, and 659; 399, 428, 484, 537, 613, and 671; 400, 450, 484, 540, 598, and 659; 401, 428, 484, 541, 591, and 659; 390, 428, 484, 542, 629, and 659; 376, 428, 484, 523, 591, and 671; 400, 428, 499, 523, 591, and 659; 381, 428, 484, 523, 630, and 667; 384, 429, 484, 543, 631, and 659; 369, 428, 484, 523, 632, and 664; 402, 436,

484, 523, 597, and 661; 381, 451, 484, 523, 591, and 656; 403, 428, 484, 523, 633, and 659; 369, 429, 484, 544, 607, and 659; 404, 429, 484, 523, 630, and 659; 372, 429, 484, 523, 602, and 659; 381, 428, 484, 523, 591, and 665; 388, 428, 484, 523, 610, and 674; 405, 451, 484, 523, 634, and 671; 406, 428, 484, 545, 591, and 661; 400, 428, 484, 523, 635, and 667; 404, 428, 484, 546, 591, and 659; 384, 432, 500, 523, 636, and 664; 376, 452, 501, 547, 591, and 663; 407, 428, 484, 548, 619, and 659; 375, 428, 484, 523, 637, and 659; 372, 428, 484, 523, 607, and 659; 408, 428, 484, 523, 638, and 659; 386, 428, 484, 523, 591, and 659; 369, 428, 497, 523, 591, and 659; 403, 453, 484, 549, 591, and 659; 402, 454, 484, 523, 591, and 659; 383, 428, 484, 523, 591, and 659; 383, 434, 500, 523, 591, and 659; 376, 455, 502, 550, 591, and 675; 383, 435, 484, 523, 591, and 664; 369, 428, 484, 523, 602, and 659; 376, 428, 484, 551, 591, and 659; 376, 428, 484, 552, 591, and 659; 383, 428, 484, 553, 591, and 676; 376, 428, 484, 554, 591, and 659; 376, 428, 490, 523, 591, and 676; 369, 428, 503, 555, 606, and 659; 409, 428, 484, 523, 591, and 659; 383, 428, 504, 556, 591, and 659; 369, 434, 484, 523, 591, and 659; 390, 428, 484, 523, 637, and 677; 369, 456, 484, 523, 591, and 659; 370, 457, 484, 557, 591, and 659; 383, 428, 484, 558, 591, and 659; 404, 458, 499, 523, 591, and 659; 410, 428, 484, 523, 591, and 677; 383, 459, 484, 553, 639, and 659; 407, 428, 489, 549, 591, and 667; 374, 434, 484, 523, 591, and 659; 404, 428, 484, 559, 617, and 666; 411, 460, 505, 523, 591, and 672; 372, 429, 484, 523, 606, and 659; 383, 428, 485, 523, 591, and 659; 386, 460, 490, 523, 601, and 659; 412, 455, 493, 523, 592, and 670; 372, 428, 484, 560, 591, and 667; 372, 428, 484, 523, 606, and 659; 383, 461, 484, 523, 591, and 677; 369, 429, 484, 523, 606, and 659; 369, 434, 484, 530, 591, and 659; 376, 437, 484, 561, 603, and 666; 383, 462, 500, 523, 591, and 659; 383, 428, 484, 562, 591, and 659; 400, 463, 484, 523, 616, and 660; 376, 464, 484, 523, 602, and 677; 400, 434, 506, 549, 591, and 659; 369, 436, 507, 523, 591, and 659; 404, 429, 484, 523, 591, and 659; 384, 429, 484, 523, 616, and 659; 369, 429, 484, 523, 591, and 659; 377, 465, 484, 523, 630, and 660; 413, 459, 484, 563, 591, and 659; 369, 452, 484, 523, 591, and 663; 414, 466, 484, 523, 640, and 659; 373, 428, 484, 523, 591, and 659; 415, 428, 489, 564, 591, and 659; 369, 428, 484, 523, 591, and 671; 400, 428, 484, 523, 641, and 677; 369, 428, 491, 565, 591, and 662; 403, 458, 508, 523, 642, and 664; 392, 467, 484, 523, 591, and 659; 369, 452, 509, 566, 643, and 659; 388, 468, 490, 523, 591, and 659; 369, 452, 484, 523, 644, and 667; 377, 440, 484, 567, 606, and 659; 370, 428, 484, 523, 591, and 656; 384, 467, 487, 523, 591, and 659; 392, 469, 510, 568, 591, and 659; 378, 464, 484, 523, 606, and 659; 377, 428, 484, 569, 645, and 659; 416, 434, 484, 523, 603, and 659; 370, 428, 484, 523, 606, and 659; 370, 428, 511, 570, 628, and

678; 369, 452, 484, 571, 630, and 663; 376, 428, 502, 572, 591, and 664; 417, 428, 484, 523, 591, and 665; 392, 428, 484, 573, 591, and 670; 376, 428, 512, 523, 646, and 659; 377, 428, 484, 574, 591, and 670; 383, 428, 484, 523, 647, and 667; 381, 428, 493, 575, 591, and 659; 383, 470, 501, 523, 591, and 659; 404, 471, 484, 537, 591, and 659; 418, 428, 484, 523, 635, and 670; 383, 472, 513, 576, 591, and 659; 419, 428, 484, 577, 606, and 659; 397, 428, 484, 523, 648, and 679; 372, 473, 484, 523, 591, and 664; 383, 474, 484, 523, 592, and 659; 372, 428, 484, 523, 591, and 663; 420, 434, 484, 523, 595, and 659; 370, 428, 514, 523, 591, and 659; 369, 428, 484, 523, 591, and 677; 383, 428, 484, 523, 600, and 659; 369, 475, 484, 523, 591, and 659; 421, 436, 484, 523, 649, and 664; 378, 452, 484, 523, 591, and 659; 376, 476, 515, 578, 641, and 659; 376, 428, 504, 523, 591, and 667; 422, 469, 484, 523, 606, and 660; 383, 461, 484, 523, 616, and 659; 369, 428, 484, 523, 650, and 656; 369, 428, 516, 523, 591, and 659; 405, 460, 484, 523, 618, and 659; 413, 431, 484, 523, 591, and 659; 382, 428, 484, 579, 621, and 671; 383, 428, 484, 523, 646, and 659; 372, 428, 484, 580, 591, and 660; 406, 429, 484, 527, 591, and 659; 383, 428, 517, 581, 595, and 659; 377, 437, 518, 582, 640, and 664; 369, 477, 487, 583, 651, and 659; 403, 464, 484, 534, 591, and 659; 383, 459, 484, 523, 606, and 659; 369, 454, 484, 584, 591, and 671; 372, 478, 519, 523, 591, and 680; 423, 429, 484, 523, 591, and 681; 383, 428, 484, 585, 591, and 659; 369, 434, 484, 557, 591, and 659; 382, 434, 484, 523, 649, and 659; 424, 479, 484, 523, 616, and 660; 376, 429, 484, 586, 591, and 666; 425, 428, 484, 523, 592, and 659; 369, 436, 484, 587, 652, and 659; 403, 428, 520, 588, 638, and 659; 417, 460, 484, 523, 591, and 659; 409, 460, 484, 523, 623, and 664; 404, 452, 484, 523, 591, and 659; 369, 428, 484, 523, 591, and 682; 383, 428, 521, 553, 653, and 659; 372, 480, 493, 523, 591, and 659; 369, 428, 484, 523, 654, and 659; 369, 477, 484, 523, 648, and 659; 369, 481, 484, 560, 591, and 659; 369, 452, 484, 523, 591, and 667; 409, 428, 484, 580, 606, and 659; 384, 452, 484, 589, 593, and 661; 377, 482, 484, 523, 591, and 659; 410, 483, 484, 523, 591, and 659; 384, 428, 489, 523, 591, and 659; 426, 429, 484, 523, 622, and 659; 376, 428, 484, 523, 637, and 676; 427, 428, 484, 523, 591, and 671; 373, 452, 506, 523, 591, and 659; 369, 428, 484, 590, 622, and 659; 369, 429, 521, 555, 591, and 661; 405, 428, 522, 523, 615, and 672; 376, 428, 510, 523, 591, and 659; 384, 428, 484, 523, 626, and 668; 410, 429, 484, 523, 591, and 659; 400, 452, 484, 523, 655, and 659; or 369, 434, 484, 523, 606, and 680.

6. The antibody of any one of the preceding claims, wherein the antibody comprises the VH amino acid sequence of any one of SEQ ID NOs: 1-180.

7. The antibody of any one of the preceding claims, wherein the antibody comprises the VL amino acid sequence of any one of SEQ ID NOs: 181-368.

8. The antibody of any one of the preceding claims, wherein the VH and VL comprise the amino acid sequences, respectively, set forth in SEQ ID NOs: 1 and 181; 2 and 182; 3 and 183; 4 and 184; 5 and 185; 1 and 184; 6 and 184; 1 and 186; 7 and 187; 8 and 188; 9 and 189; 10 and 190; 4 and 191; 11 and 192; 12 and 193; 13 and 194; 14 and 195; 15 and 196; 16 and 184; 17 and 197; 18 and 198; 1 and 199; 19 and 200; 20 and 201; 21 and 202; 22 and 203; 23 and 204; 24 and 205; 25 and 184; 4 and 206; 26 and 207; 27 and 208; 28 and 209; 9 and 210; 29 and 211; 30 and 212; 31 and 213; 32 and 214; 33 and 215; 34 and 216; 17 and 217; 1 and 218; 35 and 184; 36 and 184; 35 and 219; 35 and 220; 37 and 184; 38 and 221; 39 and 222; 9 and 223; 9 and 224; 40 and 184; 41 and 225; 8 and 226; 42 and 227; 35 and 228; 43 and 229; 4 and 230; 9 and 231; 8 and 232; 1 and 233; 8 and 234; 44 and 184; 1 and 235; 45 and 236; 30 and 237; 46 and 184; 47 and 238; 48 and 239; 1 and 230; 49 and 190; 44 and 240; 50 and 184; 51 and 241; 52 and 242; 53 and 243; 54 and 184; 55 and 244; 56 and 245; 57 and 246; 58 and 247; 59 and 248; 60 and 249; 8 and 250; 61 and 184; 35 and 251; 62 and 252; 1 and 253; 63 and 254; 64 and 181; 65 and 255; 66 and 256; 67 and 257; 68 and 198; 35 and 258; 69 and 259; 70 and 260; 71 and 261; 72 and 262; 73 and 263; 74 and 264; 75 and 265; 76 and 266; 77 and 267; 4 and 205; 78 and 268; 1 and 269; 27 and 269; 79 and 269; 80 and 270; 81 and 269; 22 and 269; 82 and 269; 83 and 271; 84 and 272; 1 and 273; 8 and 274; 8 and 275; 22 and 276; 8 and 277; 85 and 278; 86 and 279; 87 and 269; 88 and 280; 89 and 269; 60 and 281; 90 and 269; 91 and 282; 22 and 283; 92 and 269; 93 and 284; 94 and 285; 95 and 286; 96 and 269; 73 and 287; 97 and 288; 68 and 289; 98 and 269; 99 and 290; 100 and 291; 4 and 292; 4 and 289; 101 and 284; 66 and 289; 89 and 293; 102 and 294; 103 and 269; 22 and 295; 104 and 296; 105 and 297; 106 and 270; 107 and 269; 67 and 269; 62 and 298; 66 and 269; 108 and 299; 109 and 300; 110 and 301; 111 and 302; 112 and 269; 113 and 303; 1 and 304; 72 and 305; 114 and 306; 115 and 307; 116 and 269; 117 and 308; 118 and 269; 110 and 309; 119 and 310; 120 and 311; 121 and 269; 122 and 312; 123 and 289; 9 and 313; 124 and 314; 120 and 289; 125 and 315; 110 and 316; 126 and 317; 127 and 318; 49 and 319; 128 and 320; 9 and 321; 22 and 322; 129 and 323; 130 and 269; 131 and 324; 132 and 325; 133 and 326; 134 and 327; 53 and 328; 135 and 272; 136 and 329; 4 and 301; 137 and 330; 138 and 269; 1 and 284; 22 and 331;

139 and 269; 140 and 332; 141 and 269; 142 and 333; 143 and 334; 144 and 335; 101 and 298; 1 and 336; 145 and 269; 146 and 337; 147 and 269; 17 and 338; 22 and 320; 4 and 339; 148 and 340; 149 and 341; 150 and 342; 151 and 343; 152 and 344; 94 and 289; 153 and 345; 154 and 346; 155 and 347; 22 and 348; 89 and 282; 156 and 349; 157 and 296; 158 and 350; 159 and 329; 24 and 351; 160 and 352; 161 and 269; 162 and 353; 163 and 269; 1 and 354; 164 and 355; 165 and 269; 1 and 356; 166 and 357; 167 and 358; 110 and 334; 87 and 359; 168 and 360; 169 and 269; 170 and 269; 171 and 269; 172 and 361; 8 and 362; 173 and 304; 174 and 269; 1 and 363; 175 and 364; 176 and 365; 177 and 269; 178 and 366; 179 and 269; 180 and 367; or 89 and 368.

9. The antibody of any one of the preceding claims, wherein the antibody is a single-chain variable fragment (scFv).

10. The antibody of any one of claims 1-8, wherein the antibody comprises a heavy chain constant region, or an Fc region thereof, optionally selected from the group consisting of a human IgG_1, IgG_2, IgG_3, IgG_4, IgA_1, and IgA_2.

11. The antibody of claim 10, wherein the heavy chain constant region is a human IgG_1.

12. The antibody of claim 10, wherein the heavy chain constant region is a human IgG_4.

13. The antibody of claim 12, wherein the amino acid sequence of the human IgG_4 heavy chain constant region comprises a P at position 228, numbered according to the EU numbering system.

14. The antibody of any one of claims 10-13, wherein the heavy chain constant region is a variant of a wild-type heavy chain constant region, wherein the variant heavy chain constant region binds to an Fc gamma receptor (FcγR) with lower affinity than the wild-type heavy chain constant region binds to the FcγR.

15. The antibody of claim 14, wherein the amino acid sequence of the heavy chain constant region comprises: A at position 234; A at position 235; A, Q or G at position 297; or A or G at position 329, in each case numbered according to the EU numbering system.

16. The antibody of claim 14, wherein the amino acid sequence of the heavy chain constant region comprises: A at positions 234 and 235; A at positions 234, 235, and 329; or A at positions 234, 235, and G at position 329, in each case numbered according to the EU numbering system.

17. The antibody of any one of claims 10-16, wherein the heavy chain constant region is a variant of a wild-type heavy chain constant region, and wherein the variant heavy chain constant region has an increased affinity for human neonatal Fc receptor (FcRn) at pH 6 relative to the affinity of the wild-type heavy chain constant region for human FcRn at pH 6.

18. The antibody of claim 17, wherein the amino acid sequence of the heavy chain constant region comprises: L and S at positions 428 and 434, respectively; K, F, and Y at positions 433, 434, and 436, respectively; or Y, T, and E at positions 252, 254, and 256, respectively, in each case numbered according to the EU numbering system.

19. The antibody of any one of claims 1-18, comprising a light chain constant region, optionally a human kappa or lambda constant region.

20. A polypeptide comprising a VH comprising the CDRH1, CDRH2, and CDRH3 amino acid sequences of any one of the VH amino acid sequences set forth in SEQ ID NOs: 1-180.

21. The polypeptide of claim 20, wherein the polypeptide comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and 485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393,

428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and 484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

22. The polypeptide of claim 20, wherein the VH comprises the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 369, 428, and 484; 370, 429, and

485; 371, 428, and 486; 372, 428, and 484; 373, 429, and 484; 374, 430, and 484; 375, 428, and 487; 376, 428, and 484; 377, 428, and 484; 378, 428, and 484; 379, 428, and 484; 372, 428, and 488; 376, 431, and 484; 380, 432, and 484; 372, 428, and 489; 381, 428, and 490; 382, 428, and 484; 381, 428, and 491; 377, 428, and 492; 376, 433, and 484; 383, 434, and 484; 383, 428, and 484; 384, 435, and 484; 369, 436, and 484; 372, 437, and 487; 385, 428, and 493; 386, 428, and 484; 372, 437, and 484; 387, 428, and 484; 385, 428, and 484; 372, 438, and 484; 388, 428, and 494; 369, 439, and 484; 389, 428, and 484; 381, 428, and 484; 376, 440, and 495; 390, 441, and 484; 370, 442, and 484; 391, 428, and 484; 392, 432, and 484; 377, 443, and 484; 393, 428, and 484; 383, 444, and 489; 394, 428, and 484; 383, 444, and 496; 376, 434, and 484; 395, 445, and 497; 396, 446, and 487; 392, 428, and 484; 393, 428, and 498; 376, 428, and 495; 369, 440, and 484; 397, 428, and 484; 389, 447, and 484; 398, 448, and 492; 373, 449, and 490; 399, 428, and 484; 400, 450, and 484; 401, 428, and 484; 390, 428, and 484; 400, 428, and 499; 384, 429, and 484; 402, 436, and 484; 381, 451, and 484; 403, 428, and 484; 369, 429, and 484; 404, 429, and 484; 372, 429, and 484; 388, 428, and 484; 405, 451, and 484; 406, 428, and 484; 400, 428, and 484; 404, 428, and 484; 384, 432, and 500; 376, 452, and 501; 407, 428, and 484; 375, 428, and 484; 408, 428, and 484; 369, 428, and 497; 403, 453, and 484; 402, 454, and 484; 383, 434, and 500; 376, 455, and 502; 383, 435, and 484; 376, 428, and 490; 369, 428, and 503; 409, 428, and 484; 383, 428, and 504; 369, 434, and 484; 369, 456, and 484; 370, 457, and 484; 404, 458, and 499; 410, 428, and 484; 383, 459, and 484; 407, 428, and 489; 374, 434, and 484; 411, 460, and 505; 383, 428, and 485; 386, 460, and 490; 412, 455, and 493; 383, 461, and 484; 376, 437, and 484; 383, 462, and 500; 400, 463, and 484; 376, 464, and 484; 400, 434, and 506; 369, 436, and 507; 377, 465, and 484; 413, 459, and 484; 369, 452, and 484; 414, 466, and 484; 373, 428, and 484; 415, 428, and 489; 369, 428, and 491; 403, 458, and 508; 392, 467, and 484; 369, 452, and 509; 388, 468, and 490; 377, 440, and 484; 370, 428, and 484; 384, 467, and 487; 392, 469, and 510; 378, 464, and 484; 416, 434, and 484; 370, 428, and 511; 376, 428, and 502; 417, 428, and 484; 376, 428, and 512; 381, 428, and 493; 383, 470, and 501;404, 471, and 484; 418, 428, and 484; 383, 472, and 513; 419, 428, and 484; 372, 473, and 484; 383, 474, and 484; 420, 434, and 484; 370, 428, and 514; 369, 475, and 484; 421, 436, and 484; 378, 452, and 484; 376, 476, and 515; 376, 428, and 504; 422, 469, and 484; 369, 428, and 516; 405, 460, and 484; 413, 431, and 484; 406, 429, and 484; 383, 428, and 517; 377, 437, and 518; 369, 477, and 487; 403, 464, and 484; 369, 454, and 484; 372, 478, and 519; 423, 429, and 484; 382, 434, and 484; 424, 479, and

484; 376, 429, and 484; 425, 428, and 484; 403, 428, and 520; 417, 460, and 484; 409, 460, and 484; 404, 452, and 484; 383, 428, and 521; 372, 480, and 493; 369, 477, and 484; 369, 481, and 484; 384, 452, and 484; 377, 482, and 484; 410, 483, and 484; 384, 428, and 489; 426, 429, and 484; 427, 428, and 484; 373, 452, and 506; 369, 429, and 521; 405, 428, and 522; 376, 428, and 510; 384, 428, and 484; 410, 429, and 484; or 400, 452, and 484.

23. The polypeptide of claim 20, wherein the VH comprises any one of the amino acid sequences set forth in SEQ ID NOs: 1-180.

24. A polypeptide comprising a VL comprising the CDRL1, CDRL2, and CDRL3 amino acid sequences of any one of the VL amino acid sequences set forth in SEQ ID NOs: 181-368.

25. The polypeptide of claim 24, wherein the polypeptide comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and 659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523,

637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

26. The polypeptide of claim 24, wherein the VL comprises the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 523, 591, and 656; 523, 592, and 657; 523, 593, and 658; 523, 591, and 659; 523, 594, and 659; 523, 595, and 660; 523, 596, and 659; 524, 591, and 659; 523, 591, and 661; 523, 591, and 662; 523, 597, and 658; 523, 598, and 662; 525, 599, and 659; 523, 600, and 663; 523, 591, and 664; 523, 601, and 659; 526, 597, and 665; 523, 602, and 659; 527, 591, and 661; 528, 591, and 662; 529, 603, and 662; 523, 604, and 666; 523, 605, and 667; 530, 606, and 659; 523, 607, and 659; 523, 608, and 659; 523, 609, and 662; 531, 591, and 663; 523, 608, and 661; 523, 610, and 659; 523, 611, and 668; 523, 611, and 658; 523, 596, and 662; 523, 612, and 667; 523, 613, and 668; 523, 591, and 669; 523, 591, and 663; 523, 614, and 659; 532, 615, and 662; 523, 616, and 670; 523, 591, and 668; 523, 617, and 671; 533, 595, and 659; 523, 618, and 659; 534, 619, and 662; 535, 620, and 659; 536, 621, and

659; 537, 603, and 671; 523, 622, and 659; 523, 617, and 659; 523, 623, and 659; 538, 607, and 672; 523, 616, and 671; 523, 624, and 659; 523, 620, and 659; 523, 625, and 660; 523, 602, and 671; 523, 611, and 663; 523, 626, and 670; 523, 606, and 673; 523, 627, and 671; 523, 628, and 671; 539, 591, and 662; 523, 591, and 670; 523, 611, and 659; 537, 613, and 671; 540, 598, and 659; 541, 591, and 659; 542, 629, and 659; 523, 591, and 671; 523, 630, and 667; 543, 631, and 659; 523, 632, and 664; 523, 597, and 661; 523, 633, and 659; 544, 607, and 659; 523, 630, and 659; 523, 591, and 665; 523, 610, and 674; 523, 634, and 671; 545, 591, and 661; 523, 635, and 667; 546, 591, and 659; 523, 636, and 664; 547, 591, and 663; 548, 619, and 659; 523, 637, and 659; 523, 638, and 659; 549, 591, and 659; 550, 591, and 675; 551, 591, and 659; 552, 591, and 659; 553, 591, and 676; 554, 591, and 659; 523, 591, and 676; 555, 606, and 659; 556, 591, and 659; 523, 637, and 677; 557, 591, and 659; 558, 591, and 659; 523, 591, and 677; 553, 639, and 659; 549, 591, and 667; 559, 617, and 666; 523, 591, and 672; 523, 606, and 659; 523, 592, and 670; 560, 591, and 667; 530, 591, and 659; 561, 603, and 666; 562, 591, and 659; 523, 616, and 660; 523, 602, and 677; 523, 616, and 659; 523, 630, and 660; 563, 591, and 659; 523, 640, and 659; 564, 591, and 659; 523, 641, and 677; 565, 591, and 662; 523, 642, and 664; 566, 643, and 659; 523, 644, and 667; 567, 606, and 659; 568, 591, and 659; 569, 645, and 659; 523, 603, and 659; 570, 628, and 678; 571, 630, and 663; 572, 591, and 664; 573, 591, and 670; 523, 646, and 659; 574, 591, and 670; 523, 647, and 667; 575, 591, and 659; 537, 591, and 659; 523, 635, and 670; 576, 591, and 659; 577, 606, and 659; 523, 648, and 679; 523, 592, and 659; 523, 595, and 659; 523, 600, and 659; 523, 649, and 664; 578, 641, and 659; 523, 591, and 667; 523, 606, and 660; 523, 650, and 656; 579, 621, and 671; 580, 591, and 660; 527, 591, and 659; 581, 595, and 659; 582, 640, and 664; 583, 651, and 659; 534, 591, and 659; 584, 591, and 671; 523, 591, and 680; 523, 591, and 681; 585, 591, and 659; 523, 649, and 659; 586, 591, and 666; 587, 652, and 659; 588, 638, and 659; 523, 623, and 664; 523, 591, and 682; 553, 653, and 659; 523, 654, and 659; 523, 648, and 659; 560, 591, and 659; 580, 606, and 659; 589, 593, and 661; 523, 637, and 676; 590, 622, and 659; 555, 591, and 661; 523, 615, and 672; 523, 626, and 668; 523, 655, and 659; or 523, 606, and 680.

27. The polypeptide of claim 24, wherein the VL comprises any one of the amino acid sequences set forth in SEQ ID NOs: 181-368.

28. The antibody or polypeptide of any one of the preceding claims, wherein the antibody or polypeptide is conjugated to a cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.

29. A polynucleotide encoding a VH and/or a VL of an antibody of any one of claims 1-19, or a polypeptide of any one of claims 20-27.

30. A vector comprising the polynucleotide of claim 29.

31. The vector of claim 30, wherein the vector is an adeno-associated virus (AAV) vector.

32. A recombinant host cell comprising:

(a) the polynucleotide of claim 29;

(b) the vector of claim 30 or 31;

(c) a first polynucleotide encoding a VH or heavy chain of the antibody of any one of claims 1-19, and a second polynucleotide encoding a VL or light chain of the antibody of any one of claims 1-19; or

(d) a first vector comprising a first polynucleotide encoding a VH or heavy chain of the antibody of any one of claims 1-19, and a second vector comprising a second polynucleotide encoding a VL or light chain of the antibody of any one of claims 1-19.

33. A pharmaceutical composition comprising the antibody or polypeptide of any one of claims 1-28, the polynucleotide of claim 29, the vector of claim 30 or 31, or the host cell of claim 32, and a pharmaceutically acceptable carrier or excipient.

34. A method of producing an antibody or polypeptide, the method comprising culturing the host cell of claim 32 under suitable conditions such that the polynucleotide is expressed, and the antibody or polypeptide is produced.

35. A method of inhibiting an activity of PC in a subject, the method comprising administering to the subject an effective amount of the antibody or polypeptide of any one of claims 1-28, the

polynucleotide of claim 29, the vector of claim 30 or 31, the host cell of claim 32, or the pharmaceutical composition of claim 33.

36. A method of treating an inflammatory disorder or degenerative disease in a subject, the method comprising administering to the subject an effective amount of the antibody or polypeptide of any one of claims 1-28, the polynucleotide of claim 29, the vector of claim 30 or 31, the host cell of claim 32, or the pharmaceutical composition of claim 33.

37. The method of claim 36, wherein the inflammatory disorder or degenerative disease is selected from the group consisting of organ reperfusion injury such as myocardial infarction induced reperfusion injury, Kawasaki disease, non-alcoholic steatohepatitis (NASH), organ transplant rejection, atherosclerosis, Type I or Type 2 Diabetes, rheumatoid arthritis, osteoporosis, acute lung injury, asthma, chronic obstructive pulmonary disease (COPD), lung fibrosis, pain, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), age-related macular degeneration (AMD), stroke, Huntington's disease, frontotemporal dementia (FTD), multiple sclerosis (MS), isolated demyelinating diseases of the central nervous system, osteoarthritis, Crohn's Disease, and ulcerative colitis.

38. Use of the antibody or polypeptide of any one of claims 1-28, the polynucleotide of claim 29, the vector of claim 30 or 31, the host cell of claim 32, or the pharmaceutical composition of claim 33, for the manufacture of a medicament for the treatment of an inflammatory disorder or degenerative disease in a subject in need thereof.

39. The use according to claim 38, wherein the inflammatory disorder or degenerative disease is selected from the group consisting of organ reperfusion injury such as myocardial infarction induced reperfusion injury, Kawasaki disease, non-alcoholic steatohepatitis (NASH), organ transplant rejection, atherosclerosis, Type I or Type 2 Diabetes, rheumatoid arthritis, osteoporosis, acute lung injury, asthma, chronic obstructive pulmonary disease (COPD), lung fibrosis, pain, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), age-related macular degeneration (AMD), stroke, Huntington's disease, frontotemporal dementia (FTD), multiple sclerosis (MS), isolated demyelinating diseases of the central nervous system, osteoarthritis, Crohn's Disease, and

ulcerative colitis.

40. The antibody or polypeptide of any one of claims 1-28, the polynucleotide of claim 29, the vector of claim 30 or 31, the host cell of claim 32, or the pharmaceutical composition of claim 33, for use in medicine.

41. The antibody or polypeptide of any one of claims 1-28, the polynucleotide of claim 29, the vector of claim 30 or 31, the host cell of claim 32, or the pharmaceutical composition of claim 33, for use in the treatment of an inflammatory disorder or degenerative disease in a subject in need thereof.

42. The use according to claim 41, wherein the inflammatory disorder or degenerative disease is selected from the group consisting of organ reperfusion injury such as myocardial infarction induced reperfusion injury, Kawasaki disease, non-alcoholic steatohepatitis (NASH), organ transplant rejection, atherosclerosis, Type I or Type 2 Diabetes, rheumatoid arthritis, osteoporosis, acute lung injury, asthma, chronic obstructive pulmonary disease (COPD), lung fibrosis, pain, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), age-related macular degeneration (AMD), stroke, Huntington's disease, frontotemporal dementia (FTD), multiple sclerosis (MS), isolated demyelinating diseases of the central nervous system, osteoarthritis, Crohn's Disease, and ulcerative colitis.