CLAIMS

We claim:

1. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to IL-22, wherein the antibody, or antigen-binding fragment thereof, comprises an amino acid sequence which is at least 95% identical to the amino acid sequence shown in SEQ ID NO:5, 6, 7, 23, 24, 25, 41, 42, 43, 59, 60, 61, 77, 78, 79, 95, 96, 97, 113, 114, 115, 131, 132, 133, 149, 150, 151, 167, 168, 169, 185, 186, 187, 203, 204, 205, 221, 222, 223, 239, 240, 241, 257, 258, 259, 275, 276, 277, 293, 294, 295, 311, 312, 313, 329, 330, 331, 347, 348, 349, 365, 366, 367, 383, 384, 385, 401, 402, 403, 419, 420, 421, 437, 438, 439, 455, 456, 457, 473, 474, 475, 491, 492, 493, 509, 510, 511, 527, 528, 529, 545, 546, 547, 563, 564, 565, 581, 582, 583, 599, 600, 601, 617, 618, or 619.

2. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to IL-22, wherein the antibody, or antigen-binding fragment thereof, comprises an amino acid sequence encoded by a nucleotide sequence which is at least 95% identical to the nucleotide sequence shown in SEQ ID NO:14, 15, 16, 32, 33, 34, 50, 51, 52, 68, 69, 70, 86, 87, 88, 104, 105, 106, 122, 123, 124, 140, 141, 142, 158, 159, 160, 176, 177, 178, 194, 195, 196, 212, 213, 214, 230, 231, 232, 248, 249, 250, 266, 267, 268, 284, 285, 286, 302, 303, 304, 320, 321, 322, 338, 339, 340, 356, 357, 358, 374, 375, 376, 392, 393, 394, 410, 411, 412, 428, 429, 430, 446, 447, 448, 464, 465, 466, 482, 483, 484, 500, 501, 502, 518, 519, 520, 536, 537, 538, 554, 555, 556, 572, 573, 574, 590, 591, 592, 608, 609, 610, 626, 627, or 628.

3. The antibody of claim 1, comprising the amino acid sequence as set out in SEQ ID NO:5, 6, 7, 23, 24, 25, 41, 42, 43, 59, 60, 61, 77, 78, 79, 95, 96, 97, 113, 114, 115, 131, 132, 133, 149, 150, 151, 167, 168, 169, 185, 186, 187, 203, 204, 205, 221, 222, 223, 239, 240, 241, 257, 258, 259, 275, 276, 277, 293, 294, 295, 311, 312, 313, 329, 330, 331, 347, 348, 349, 365, 366, 367, 383, 384, 385, 401, 402, 403, 419, 420, 421, 437, 438, 439, 455, 456, 457, 473, 474, 475, 491, 492, 493, 509, 510, 511, 527, 528, 529, 545, 546, 547, 563, 564, 565, 581, 582, 583, 599, 600, 601, 617, 618, or 619.

4. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to IL-22, wherein the antibody, or antigen-binding fragment thereof, comprises a V_L domain having a light chain variable region and a V_H domain having a heavy chain variable region, wherein the heavy chain variable region comprises one or more of SEQ ID NO:8, 9, 10, 26, 27, 28, 44, 45, 46, 62, 63, 64, 80, 81, 82, 98, 99, 100, 116, 117, 118, 134, 135, 136, 152, 153, 154, 170, 171, 172, 188, 189, 190, 206, 207, 208, 224, 225, 226, 242, 243, 244, 260, 261, 262, 278, 279, 280, 296, 297, 298, 314, 315, 316, 332, 333, 334, 350, 351, 352, 368, 369, 370, 386, 387, 388, 404, 405, 406, 422, 423, 424, 440, 441, 442, 458, 459, 460, 476, 477, 478, 494, 495, 496, 512, 513, 514, 530, 531, 532, 548, 549, 550, 566, 567, 568, 584, 585, 586, 602, 603, 604, 620, 621, or 622.

5. The antibody of claim 4, wherein the light chain variable region comprises one or more of SEQ ID NO:11, 12, 13, 29, 30, 31, 47, 48, 49, 65, 66, 67, 83, 84, 85, 101, 102, 103, 119, 120, 121, 137, 138, 139, 155, 156, 157, 173, 174, 175, 191, 192, 193, 209, 210, 211, 227, 228, 229, 245, 246, 247, 263, 264, 265, 281, 282, 283, 299, 300, 301, 317, 318, 319, 335, 336, 337, 353, 354, 355, 371, 372, 373, 389, 390, 391, 407, 408, 409, 425, 426, 427, 443, 444, 445, 461, 462, 463, 479, 480, 481, 497, 498, 499, 515, 516, 517, 533, 534, 535, 551, 552, 553, 569, 570, 571, 587, 588, 589, 605, 606, 607, 623, 624, and 625.

6. The antibody of claim 5, wherein the V_H domain comprises the amino acid sequence of any one of SEQ ID NO:5, 23, 41, 59, 77, 95, 113, 131, 149, 167, 185, 203, 221, 239, 257, 275, 293, 311, 329, 347, 365, 383, 401, 419, 437, 455, 473, 491, 509, 527, 545, 563, 581, 599, or 617 and the V_L domain comprises the amino acid sequence of any one of SEQ ID NO:6, 24, 42, 60, 78, 96, 114, 132, 150, 168, 186, 204, 222, 240, 258, 276, 294, 312, 330, 348, 366, 384, 402, 420, 438, 456, 474, 492, 510, 528, 546, 564, 582, 600, or 618.

7. The antibody of claim 6, wherein:

a) the V_H domain comprises the amino acid sequence set out in SEQ ID NO:167 or 491; and

b) the V_L domain comprises the amino acid sequence set out in SEQ ID NO:168 or 492.

8. The antibody of claim 6, wherein:

a) the V_H domain comprises the amino acid sequence set out in SEQ ID NO:293 or 545; and

b) the V_L domain comprises the amino acid sequence set out in SEQ ID NO:294 or 546.

9. The antibody of claim 6, wherein:

a) the V_H domain comprises the amino acid sequence set out in SEQ ID NO:203 or 617; and

b) the V_L domain comprises the amino acid sequence set out in SEQ ID NO:204 or 618.

10. The antibody of claim 6, wherein:

a) the V_H domain comprises the amino acid sequence set out in SEQ ID NO:347 or 599; and

b) the V_L domain comprises the amino acid sequence set out in SEQ ID NO:348 or 600.

11. The antibody of claim 4, wherein the heavy chain variable region comprises:

a) SEQ ID NO:170 or 494,

b) SEQ ID NO:171 or 495; and

c) SEQ ID NO:172 or 496.

12. The antibody of claim 4, wherein the heavy chain variable region comprises:

a) SEQ ID NO:296 or 548,

b) SEQ ID NO:297 or 549; and

c) SEQ ID NO:298 or 550.

13. The antibody of claim 4, wherein the heavy chain variable region comprises:

a) SEQ ID NO:206 or 620,

b) SEQ ID NO:207 or 621; and

c) SEQ ID NO:208 or 622.

14. The antibody of claim 4, wherein the heavy chain variable region comprises:

a) SEQ ID NO:350 or 602,

b) SEQ ID NO:351 or 603; and

c) SEQ ID NO:352 or 604.

15. The antibody of claim 11, wherein the light chain variable region comprises:

a) SEQ ID NO:173 or 497,

b) SEQ ID NO:174 or 498; and

c) SEQ ID NO:175 or 499.

16. The antibody of claim 12, wherein the light chain variable region comprises:

a) SEQ ID NO:299 or 551,

b) SEQ ID NO:300 or 552; and

c) SEQ ID NO:301 or 553.

17. The antibody of claim 13, wherein the light chain variable region comprises:

a) SEQ ID NO:209 or 623,

b) SEQ ID NO:210 or 624; and

c) SEQ ID NO:211 or 625.

18. The antibody of claim 14, wherein the light chain variable region comprises:

a) SEQ ID NO:353 or 605,

b) SEQ ID NO:354 or 606; and

c) SEQ ID NO:355 or 607.

19. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to an IL-22 epitope that is recognized by GIL01, GIL16, GIL45, GIL60, GIL68, GIL92, 097D09, 062A09, 062G05, 087B03, 367D04, 368D04, 166B06, 166G05, 375G06, 376B10, 354A08, 355B06, 355E04, or 356A11, such that the antibody competitively inhibits the binding of GIL01, GIL16, GIL45, GIL60, GIL68, GIL92, 097D09, 062A09, 062G05, 087B03, 367D04, 368D04, 166B06, 166G05, 375G06, 376B10, 354A08, 355B06, 355E04, or 356A11 to human IL-22.

20. The antibody of claim 19, comprising a V_H domain, a V_L domain, or a F_v fragment as set out in SEQ ID NO:5, 6, 7, 23, 24, 25, 41, 42, 43, 59, 60, 61, 77, 78, 79, 95, 96, 97, 113, 114, 115, 131, 132, 133, 149, 150, 151, 167, 168, 169, 185, 186, 187, 203, 204, 205, 221, 222, 223, 239, 240, 241, 257, 258, 259, 275, 276, 277, 293, 294, 295, 311, 312, 313, 329, 330, 331, 347, 348, 349, 365, 366, 367, 383, 384, 385, 401, 402, 403, 419, 420, 421, 437, 438, 439, 455, 456, 457, 473, 474, 475, 491, 492, 493, 509, 510, 511, 527, 528, 529, 545, 546, 547, 563, 564, 565, 581, 582, 583, 599, 600, 601, 617, 618, or 619.

21. The antibody of claim 20, wherein the V_H domain comprises SEQ ID NO:167 or 491.

22. The antibody of claim 21, wherein the V_L domain comprises SEQ ID NO:168 or 492.

23. The antibody of claim 20, wherein the V_H domain comprises SEQ ID NO:293 or 545.

24. The antibody of claim 23, wherein the V_L domain comprises SEQ ID NO:294 or 546.

25. The antibody of claim 20, wherein the V_H domain comprises SEQ ID NO:203 or 617.

26. The antibody of claim 25, wherein the V_L domain comprises SEQ ID NO:204 or 618.

27. The antibody of claim 20, wherein the V_H domain comprises SEQ ID NO:347 or 599.

28. The antibody of claim 27, wherein the V_L domain comprises SEQ ID NO:348 or 600.

29. The antibody of claim 19 that specifically binds to an IL-22 epitope that is recognized by 087B03, such that the antibody competitively inhibits the binding of 087B03 to human IL-22.

30. The antibody of claim 19 that specifically binds to an IL-22 epitope that is recognized by 354A08, such that the antibody competitively inhibits the binding of 354A08 to human IL-22.

31. The antibody of claim 19 that specifically binds to an IL-22 epitope that is recognized by 368D04, such that the antibody competitively inhibits the binding of 368D04 to human IL-22.

32. The antibody of claim 19 that specifically binds to an IL-22 epitope that is recognized by 356A11, such that the antibody competitively inhibits the binding of 356A11 to human IL-22.

33. The antibody of claim 22, wherein the antibody is 087B03.

34. The antibody of claim 24, wherein the antibody is 354A08.

35. The antibody of claim 26, wherein the antibody is 368D04.

36. The antibody of claim 28, wherein the antibody is 356A11.

37. The antibody of claim 1or 2, wherein the association constant of the antibody for human IL-22 is at least 10^{10} M^{-1}.

38. The antibody of claim 1 or 2, wherein the antibody blocks IL-22 mediated proliferation of BaF3 cells with an IC_{50} of 150 pM or less and wherein the BaF3 cells comprise a human IL-22 receptor.

39. The antibody of claim 1 or 2, wherein the antibody blocks IL-22 mediated GROa secretion from HT29 cells with an IC_{50} of 150 pM or less.

40. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to IL-22, wherein the association constant of the antibody for human IL-22 is at least 10^{10} M^{-1}.

41. An isolated antibody, or antigen-binding fragment thereof, wherein the antibody blocks IL-22 mediated proliferation of BaF3 cells with an IC_{50} of 150 pM or less and wherein the BaF3 cells comprise a human IL-22 receptor.

42. The antibody of claim 1 or 2, wherein the antibody specifically binds to an amino acid sequence that is at least 95% identical to any sequence of at least 100 contiguous amino acids in the sequence set forth SEQ ID NO:1.

43. The antibody of claim 1 or 2, wherein the antibody inhibits the binding of IL-22 to IL-22R or a receptor complex comprising IL-22R and IL-10R2.

44. The antibody of claim 1 or 2, wherein the antibody is human.

45. The antibody of claim 1 or 2, wherein the antibody is IgG1 or IgG4.

46. A pharmaceutical composition comprising the antibody of claim 1 or 2.

47. An isolated nucleic acid encoding the antibody of claim 1 or 2.

48. An expression vector comprising the nucleic acid of claim 47.

49. A host cell transformed with the vector of claim 48.

50. The host cell of claim 49, wherein the host cell is a bacteria, mammalian cell, yeast cell, plant cell, or an insect cell.

51. A method of producing an antibody that binds to IL-22, comprising culturing the host cell of claim 50 under conditions that allow expression of the antibody, and isolating the antibody from the cell culture.

52. The nucleic acid of claim 47, wherein the nucleic acid encodes a protein comprising an amino acid sequence set out in one of SEQ ID NO:5-13, 23-31, 41-49, 59-67, 77-85, 95-103, 113-121, 131-139, 149-157, 167-175, 185-193, 203-211, 221-229, 239-247, 257-265, 275-283, 293-301, 311-319, 329-337, 347-355, 365-373, 383-391, 401-409, 419-427, 437-445, 455-463, 473-481, 491-499, 509-517, 527-535, 545-553, 563-571, 581-589, 599-607, or 617-625.

53. The nucleic acid of claim 52, wherein the nucleic acid comprises a nucleotide sequence of one of SEQ ID NO:14-22, 32-40, 50-58, 68-76, 86-94, 104-112, 122-130, 140-148, 158-166, 176-184, 194-202, 212-220, 230-238, 248-256, 266-274, 284-292, 302-310, 320-328, 338-346, 356-364, 374-382, 392-400, 410-418, 428-436, 446-454, 464-472, 482-490, 500-508, 518-526, 536-544, 554-562, 572-580, 590-598, 608-616, or 626-634.

54. The nucleic acid of claim 52, wherein the nucleic acid encodes a protein comprising an amino acid sequence set out in SEQ ID NO:167, 168, 169, 170, 171, 172, 173, 174, 175, 491, 492, 493, 494, 495, 496, 497, 498, or 499.

55. The nucleic acid of claim 52, wherein the nucleic acid encodes a protein comprising an amino acid sequence set out in SEQ ID NO:293, 294, 295, 296, 297, 298, 299, 300, 301, 545, 546, 547, 548, 549, 550, 551, 552, or 553.

56. The nucleic acid of claim 52, wherein the nucleic acid encodes a protein comprising an amino acid sequence set out in SEQ ID NO:203, 204, 205, 206, 207, 208, 209, 210, 211, 617, 618, 619, 620, 621, 622, 623, 624, or 625.

57. The nucleic acid of claim 52, wherein the nucleic acid encodes a protein comprising an amino acid sequence set out in SEQ ID NO:347, 348, 349, 350, 351, 352, 353, 354, 355, 599, 600, 601, 602, 603, 604, 605, 606, or 607.

58. The nucleic acid of claim 53, wherein the the nucleic acid comprises a nucleotide sequence of SEQ ID NO:176, 177, 178, 179, 180, 181, 182, 183, 184, 500, 501, 502, 503, 504, 505, 506, 507, or 508.

59. The nucleic acid of claim 53, wherein the the nucleic acid comprises a nucleotide sequence of SEQ ID NO:302, 303, 304, 305, 306, 307, 308, 309, 310, 554, 555, 556, 557, 558, 559, 560, 561, or 562.

60. The nucleic acid of claim 53, wherein the the nucleic acid comprises a nucleotide sequence of SEQ ID NO:212, 213, 214, 215, 216, 217, 218, 219, 220, 626, 627, 628, 629, 630, 631, 632, 633, or 634.

61. The nucleic acid of claim 53, wherein the the nucleic acid comprises a nucleotide sequence of SEQ ID NO:356, 357, 358, 359, 360, 361, 362, 363, 364, 608, 609, 610, 611, 612, 613, 614, 615, or 616.

62. A diagnostic kit comprising the antibody of claim 1 or 2.

CLAIMS

1. An antibody, or antigen-binding fragment thereof, that specifically binds to human IL-22, wherein the antibody, or antigen-binding fragment thereof, comprises:

(a) a VH domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:23 and a VL domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:24;

(b) a VH domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:59 and a VL domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:60;

(c) a VH domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:77 and a VL domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:78; or

(d) a VH domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:95 and a VL domain comprising an amino acid sequence which is at least 90% identical to the amino acid sequence set out in SEQ ID NO:96;

and wherein (i) the association constant of the antibody for human IL-22 is at least 1010 M-1 as measured by real-time biospecific interaction analysis using surface plasmon resonance technology, (ii) the antibody blocks IL-22 mediated proliferation of BaF3 cells with an IC50 of 150 pM or less and wherein the BaF3 cells comprise a human IL-22 receptor; or (iii) the antibody blocks IL-22 mediated GROa secretion from HT29 cells with an IC50 of 150 pM or less.

2. The antibody of claim 1(a), wherein:

a) the VH domain comprises the amino acid sequence set out in SEQ ID NO:131 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:132; or

b) the VH domain comprises the amino acid sequence set out in SEQ ID NO:149 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:150.

3. The antibody of claim 1(b), wherein:

a) the VH domain comprises the amino acid sequence set out in SEQ ID NO:617 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:618;

b) the VH domain comprises the amino acid sequence set out in SEQ ID NO:491 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:492;

c) the VH domain comprises the amino acid sequence set out in SEQ ID NO:167 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:168;

d) the VH domain comprises the amino acid sequence set out in SEQ ID NO:185 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:186; or

e) the VH domain comprises the amino acid sequence set out in SEQ ID NO:203 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:204.

4. The antibody of claim 1(c), wherein:

a) the VH domain comprises the amino acid sequence set out in SEQ ID NO:527 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:528;

b) the VH domain comprises the amino acid sequence set out in SEQ ID NO:221 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:222

c) the VH domain comprises the amino acid sequence set out in SEQ ID NO:239 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:240;

d) the VH domain comprises the amino acid sequence set out in SEQ ID NO:257 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:258; or

e) the VH domain comprises the amino acid sequence set out in SEQ ID NO:275 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:276.

5. The antibody of claim 1(d), wherein:

a) the VH domain comprises the amino acid sequence set out in SEQ ID NO:599 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:600;

b) the VH domain comprises the amino acid sequence set out in SEQ ID NO:581 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:582;

c) the VH domain comprises the amino acid sequence set out in SEQ ID NO:563 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:564; or

d) the VH domain comprises the amino acid sequence set out in SEQ ID NO:545 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:546.

6. The antibody of claim 3, wherein the VH domain comprises the amino acid sequence set out in SEQ ID NO:617 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:618.

7. The antibody of claim 5, wherein the VH domain comprises the amino acid sequence set out in SEQ ID NO:599 and the VL domain comprises the amino acid sequence set out in SEQ ID NO:600.

8. An antibody, or antigen-binding fragment thereof, that specifically binds to human IL-22, wherein the antibody, or antigen-binding fragment thereof, comprises:

(a) a VH domain comprising three complementary determining regions (CDRs) comprising amino acid sequences that are substantially identical to the amino acid sequences of SEQ ID NO:602, SEQ ID NO:603, and SEQ ID NO:604 and a VL domain comprising three CDRs comprising amino acid

sequences that are substantially identical to the amino acid sequences of SEQ ID NO:605, SEQ ID NO:606, and SEQ ID NO:607; or

(b) a VH domain comprising three CDRs comprising amino acid sequences that are substantially identical to the amino acid sequences of SEQ ID NO:620, SEQ ID NO:621, and SEQ ID NO:622 and a VL domain comprising three CDRs comprising amino acid sequences that are substantially identical to the amino acid sequences of SEQ ID NO:623, SEQ ID NO:624, and SEQ ID NO:625.

9. The antibody of claim 8, wherein:

(a) the V_H domain comprises three CDRs comprising amino acid sequences that differ by one or two amino acids from at least one of the amino acid sequences of SEQ ID NO:602, SEQ ID NO:603, and SEQ ID NO:604 and the V_L domain comprises three CDRs comprising amino acid sequences that differ by one or two amino acids from at least one of the amino acid sequences of SEQ ID NO:605, SEQ ID NO:606, and SEQ ID NO:607; or

(b) the V_H domain comprises three CDRs comprising amino acid sequences that differ by one or two amino acids from at least one of the amino acid sequences of SEQ ID NO:620, SEQ ID NO:621, and SEQ ID NO:622 and the V_L domain comprises three CDRs comprising amino acid sequences that differ by one or two amino acids from at least one of the amino acid sequences of SEQ ID NO:623, SEQ ID NO:624, and SEQ ID NO:625.

10. The antibody of claim 8, wherein:

(a) the V_H domain comprises three CDRs comprising the amino acid sequences of SEQ ID NO:602, SEQ ID NO:603, and SEQ ID NO:604 and the V_L domain comprises three CDRs comprising the amino acid sequences of SEQ ID NO:605, SEQ ID NO:606, and SEQ ID NO:607; or

(b) the V_H domain comprises three CDRs comprising the amino acid sequences of SEQ ID NO:620, SEQ ID NO:621, and SEQ ID NO:622 and the V_L domain comprises three CDRs comprising the amino acid sequences of SEQ ID NO:623, SEQ ID NO:624, and SEQ ID NO:625.

11. The antibody of any one of claims 1-10, wherein:

(a) the antibody inhibits the binding of IL-22 to IL-22R or a receptor complex comprising IL-22R and IL-10R2;

(b) the antibody is human; or

(c) the antibody is IgGl or IgG4.

12. A pharmaceutical composition comprising the antibody of any one of claims 1-11.

13. An isolated nucleic acid encoding the antibody of any one of claims 1-10.

14. An expression vector comprising the nucleic acid of claim 13.

15. A host cell transformed with the vector of claim 14.

16. The host cell of claim 15, wherein the host cell is a bacterium, mammalian cell, yeast cell, plant cell, or an insect cell.

17. A method of producing an antibody that binds to IL-22, comprising culturing the host cell of claim 16 under conditions that allow expression of the antibody, and isolating the antibody from the cell culture.

18. A diagnostic kit comprising the antibody of any one of claims 1-11.