

using mice having an IL-10R1 knockout in myeloid cells showed that anti-inflammatory activity of IL-10 on myeloid cells is important for controlling colitis development (Zigmond et al., Immunity, 40(5):720-33, 2014).

SUMMARY OF THE DISCLOSURE

[0005] The present disclosure provides muteins of IL-10 that are stable as monomers and are useful in the treatment of inflammatory diseases. It is contemplated that the IL-10 muteins retain/restore IL-10 suppression activity on monocytes and macrophages, and reduce IL-10 stimulation of CD8+ T cells and B cells. The disclosure also provides antibodies to TREM-1 that are useful in the treatment of inflammatory diseases. In a further aspectexample, the disclosure provides antigen binding proteins comprising IL-10 muteins and antigen binding moieties, such as anti-TREM-1 or anti-PD-1 antibodies, useful to treat inflammatory diseases.

[0006] Provided herein is a human interleukin-10 (IL-10) mutein comprising an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 2, wherein said IL-10 mutein has at least one mutation selected from a mutation in helical loop AB, helical loop CD, helical loop DE, helix A, helix B, helix C, helix D, helix E and/or helix F. In various embodimentexamples, the IL-10 mutein of the disclosure comprises at least one mutation in helix A, helix F or helical loop AB. In various embodimentexamples, the IL-10 mutein is at least 95% identical to the amino acid sequence set forth in SEQ ID NO: 2. In various embodimentexamples, the IL-10 mutein amino acid sequence is 96%, 97%, 98% or 99% identical to the amino acid sequence set out in SEQ ID NO: 2.

[0007] In various embodimentexamples, the IL-10 mutein comprises a mutation in one or more of residues N10, H14, F15, P20, M22, L23, R24, R27, D28, K34, T35, Q38, M39, K40, D41, Q42, L43, D44, N45, L46, L47, L48, K49, F56, K57, Y59, L60, Q63, E67, Q70, M77, Q79, N82, Q83, D84, P85, D86, I87, A89, H90, S93, T100, L103, H109, R110, L112, E115, N116, A127, K130, I136, Y137, K138, S141, E142, D144, I145, E151, M154, M156, K157, or N160 of SEQ ID NO: 2 and/or an addition of 4 to 8 amino acids between helix D and helix E. In various embodimentexamples, the mutation is R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, or I87A of SEQ ID NO: 2, optionally comprising addition of 6 amino acids between helix D and helix E. In various embodimentexamples, the mutation is N10Q, N10I, N10K, R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, I87A, H14Q, F15Y, M22V, K49T, K49S, F56Y, K57N, Y59T, L60Q, Q63E, Q63L, E67C, Q70E, Q70K, M77R, M77V, Q79R, Q79C, D84R, A89P, H90E, H90Q, S93E, S93Q, T100R, L103E, H109D, R110P, R110Q, L112V, E115K, N116D,

N116Q, A127M, K130Q, I136C, Y137C, M154V, M156C, K157N, or N160D of SEQ ID NO: 2, optionally comprising addition of 4 to 8 amino acids between helix D and helix E. In various embodimentexamples, the IL10 mutein encompasses combinations of IL10 mutations as set out in Table 16 or Table 17 or Table 21, and the disclosure herein. In various embodimentexamples, the amino acids between helix D and helix E are GGGSGG (SEQ ID NO: 2676). In various embodimentexamples, the amino acid sequence of certain IL-10 muteins is set out in SEQ ID NOS: 3-10, and SEQ ID NOS: 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170 2172, 2174, 2176, 2178, 2180, 2182, 2360, 2362, 2364, 2366, 2368, 2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436, 2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2540, and 2777-2791.

[0008] In various embodimentexamples, the disclosure provides a human interleukin-10 (IL-10) mutein comprising an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in SEQ ID NOS: 3-10 or SEQ ID NOS: 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170 2172, 2174, 2176, 2178, 2180, 2182, 2360, 2362, 2364, 2366, 2368, 2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436, 2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2538, or 2540 and 2777-2791. In various embodimentexamples, the mutein comprises an amino acid sequence that is at least 95%, 96%, 97%, 98%, or 99% identical to the mutein sequences described herein.

[0009] In various embodimentexamples, the IL-10 mutein reduces the suppression of TNF- α production in myeloid cells, reduces levels of CD8+ T cell stimulation, and/or reduces the level of B cell stimulation compared to wild type (wt) IL-10. In various embodimentexamples, the anti-TREM-1/IL-10 mutein antigen binding protein suppresses TNF- α production in myeloid cells. In various embodimentexamples, the anti-TREM-1/IL-10 mutein antigen binding protein suppresses TNF- α production in myeloid cells, while reducing CD8+ T cell and B cell activation.

[0010] In various embodimentexamples, the IL-10 mutein is fused to a binding moiety that targets the antigen binding protein to myeloid cells, B cells, or T cells. In various embodimentexamples, the binding protein binds to a cell surface protein on a myeloid cell, CD8+ T cell, CD4+ T cell, or B cell.

[0011] In various embodimentexamples, the IL-10 mutein further comprises a half-life extending moiety. In various embodimentexamples, the half-life extending moiety is an Fc domain. In various embodimentexamples, the half-life extending moiety is polyethylene glycol (PEG) or the like.

[0012] In various embodimentexamples, the mutein is a dimer. In various embodimentexamples the mutein dimer comprises two different mutein monomers. In various embodimentexamples, the mutein dimer comprises the same mutein monomers.

[0013] Further provided is an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the IL-10 mutein as described herein. In various embodimentexamples, the polynucleotide sequence of the IL-10 muteins is set out in SEQ ID NO: 11-18.

[0014] The disclosure also contemplates an expression vector comprising a nucleic acid molecule comprising a nucleotide sequence that encodes the IL-10 mutein operably linked to an expression control sequence.

[0015] Provided herein is a recombinant host cell comprising the nucleic acid or vector comprising a nucleotide sequence that encodes the IL-10 mutein. In various embodimentexamples, the host cell is a mammalian cell. In various embodimentexamples, the host cell is a CHO cell. Also provided is a method of using the host cell to produce an IL-10 mutein, comprising culturing the host cell and recovering the IL-10 mutein, and an IL-10 mutein produced by the method.

[0016] The disclosure also provides a pharmaceutical composition comprising the IL-10 mutein as described herein and a pharmaceutically acceptable carrier. It is contemplated that the pharmaceutical composition can be a sterile pharmaceutical composition.

[0017] In another aspectexample, the disclosure provides an isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TrlGering Receptor Expressed on Myeloid cells 1 (TREM-1) having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 30, 50, 70, 90, 110, 130, 150, 170, 190, 210, 230, 250, 270, 290 and 2190;

- ii. a light chain CDR2 comprising an amino acid sequence selected from SEQ ID NOS: 31, 51, 71, 91, 111, 131, 151, 171, 191, 211, 231, 251, 271, 291 and 2191;
- iii. a light chain CDR3 comprising an amino acid sequence selected from SEQ ID NOS: 32, 52, 72, 92, 112, 132, 152, 172, 192, 212, 232, 252, 272, 292 and 2192;
- and
- d. comprises a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 36, 56, 76, 96, 116, 136, 156, 176, 196, 216, 236, 256, 276, 296 and 2196;
 - ii. a heavy chain CDR2 comprising an amino acid sequence selected from SEQ ID NOS: 37, 57, 77, 97, 117, 137, 157, 177, 197, 217, 237, 257, 277, 297 and 2197;
 - and
 - iii. a heavy chain CDR3 comprising an amino acid sequence selected from SEQ ID NOS: 38, 58, 78, 98, 118, 138, 158, 178, 198, 218, 238, 258, 278, 298 and 2198.

[0018] In various ~~embodiment~~examples,

- a. the light chain CDR1 sequence is set out in SEQ ID NO: 30, 50, 70, 110, 150, 170, or 290;
- b. the light chain CDR2 sequence is set out in SEQ ID NO: 31, 51, 71, 111, 151, 171, or 291;
- c. the light chain CDR3 sequence is set out in SEQ ID NO: 32, 52, 72, 112, 152, 172, or 292
- d. the heavy chain CDR1 sequence is set out in SEQ ID NO: 36, 56, 76, 116, 156, 176, or 296 ;
- e. the heavy chain CDR2 sequence is set out in SEQ ID NO: 37, 57, 77, 117, 157, 177, or 297; and
- f. the heavy chain CDR3 sequence is set out in SEQ ID NO: 38, 58, 78, 118, 158, 178, or 298.

[0019] In various ~~embodiment~~examples,

- a. the light chain CDR1 sequence is set out in SEQ ID NO: 50 or 110;
- b. the light chain CDR2 sequence is set out in SEQ ID NO: 51 or 111;
- c. the light chain CDR3 sequence is set out in SEQ ID NO: 52 or 112;
- d. the heavy chain CDR1 sequence is set out in SEQ ID NO: 56 or 116;
- e. the heavy chain CDR2 sequence is set out in SEQ ID NO: 57 or 117; and
- f. the heavy chain CDR3 sequence is set out in SEQ ID NOS: 58 or 118.

[0020] Also contemplated are consensus sequences of the TREM-1 antibody heavy and light chain CDRs and/or variable region sequences disclosed herein. For example, in various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a light chain variable region comprising a LCDR1 amino acid sequence selected from the group consisting of:

X₁ASQSX₂X₃X₄NLA (SEQ ID NO: 2199), wherein X₁ is R or Q, wherein X₂ is V or I, wherein X₃ is N or S, and wherein X₄ is S, H, I, V or A;

QASX₁DIX₂X₃X₄LN (SEQ ID NO: 2204), wherein X₁ is R or Q, wherein X₂ is R, S, N or F, wherein X₃ is K or N, and wherein X₄ is H, Y or D;

RASQSVNSNLA (SEQ ID NO: 2212);

QASQDIRKHLN (SEQ ID NO: 2213);

RASQDISSNLN (SEQ ID NO: 2214);

QASQDIHLN (SEQ ID NO: 2215);

RASQGIRKWLA (SEQ ID NO: 2216)

RASQSVNSNLA (SEQ ID NO: 2217) and

SGDKLGERVS (SEQ ID NO: 2218).

[0021] In various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a light chain variable region comprising a LCDR2 amino acid sequence selected from the group consisting of:

GAX₁X₂RAT (SEQ ID NO: 2200), wherein X₁ is S or Y, and wherein X₂ is T or I;

X₁X₂X₃X₄LET (SEQ ID NO: 2206), wherein X₁ is D, G or H, wherein X₂ is A, V or T, wherein X₃ is S, A or Y, and wherein X₄ is T or N;

GASTRAT (SEQ ID NO: 2219);

DASNLET (SEQ ID NO: 2220); and

AASRLQS (SEQ ID NO: 2221).

[0022] In various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a light chain variable region comprising a LCDR3 amino acid sequence selected from the group consisting of

QX₁X₂X₃X₄X₅X₆PX₇T (SEQ ID NO: 2201); wherein X₁ is Q, H or E, wherein X₂ is F or Y, wherein X₃ is K, Y or I, wherein X₄ is N, T, L, I, or M; wherein X₅ is W, F, H or Y, wherein X₆ is absent or P; wherein X₇ is W, N, Y, H or L;

~~QX₁YX₂X₃X₄PX₅TQX₆YX₇X₈X₉PX₁₀T~~ (SEQ ID NO: 2207), wherein X₁ is Q or H, wherein X₂ is D, A or G, wherein X₃ is N or K; wherein X₄ is L or I, and wherein X₅ is I or L;

QQFKNWPPT (SEQ ID NO: 2222);

QHYDNLPIIT (SEQ ID NO: 2223);

LQAHGFPWT (SEQ ID NO: 2224);

QQYDNLPLT (SEQ ID NO: 2225) and

QFWPPWT (SEQ ID NO: 2226).

[0023] In various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR1 amino acid sequence selected from the group consisting of:

X₁X₂X₃MX₄ (SEQ ID NO: 2202), wherein X₁ is A, R, T or S, wherein X₂ is Y or N, wherein X₃ is A or W, and wherein X₄ is S or N;

X₁YDIN (SEQ ID NO: 2208), wherein X₁ is R or S; GYYX₁H (SEQ ID NO: 2723), wherein X₁ is M or I;

AYAMS (SEQ ID NO: 2227);

RYDIN (SEQ ID NO: 2228); and

SYWMS (SEQ ID NO: 2229).

[0024] In various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR2 amino acid sequence selected from the group consisting of:

X₁X₂X₃X₄X₅X₆X₇X₈X₉YYX₁₀X₁₁X₁₂VKG (SEQ ID NO: 2205), wherein X₁ is T, E, or S, wherein X₂ is absent or is M, V, or I, wherein X₃ is S, R or K, wherein X₄ is G or Q, wherein X₅ is S, D or H, wherein X₆ is G, S L, or A, wherein X₇ is S, G, or R, wherein X₈ is T, S, P or E, wherein X₉ is T or I, wherein X₁₀ is A or V, wherein X₁₁ is D or E, and wherein X₁₂ is S or A;

X₁X₂NPX₃X₄GX₅X₆GX₇X₈X₉X₁₀FX₁₁X₁₂ (SEQ ID NO: 2209), wherein X₁ is W or R, wherein X₂ is M or L, wherein X₃ is N, Q, or K, wherein X₄ is S, A, or R, wherein X₅ is N, or Q,

wherein X₆ is S, A, or T, wherein X₇ is S, Q, or Y, wherein X₈ is V or T, wherein X₉ is Q or K, wherein X₁₀ is K or N, wherein X₁₁ is R or Q, and wherein X₁₂ is G or D;

TSGSGSTTYADSVKG (SEQ ID NO: 2230);

WMNPNSGNSSVQKFRG (SEQ ID NO: 2231);

NIKQDGSEYYVDSVKG (SEQ ID NO: 2232); and

TSGSGTTYADSVKG (SEQ ID NO: 2669).

[0025] In various ~~embodiment~~examples, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR3 amino acid sequence selected from the group consisting of:

X₁X₂X₃X₄X₅X₆ X₇ F X₈YYX₉ (SEQ ID NO: 2203), wherein X₁ is V, E, A or G, wherein X₂ is A, F, Y or G, wherein X₃ is G, S, Y or W, wherein X₄ is S or R, wherein X₅ is absent or is N, wherein X₆ is F, S, Y, or absent, wherein X₇ is L or F or absent, wherein X₈ is D or E, and wherein X₉ is Y, H or S;

X₁X₂X₃X₄ X₅X₆ X₇X₈ X₉X₁₀X₁₁X₁₂FX₁₃X₁₄ (SEQ ID NO: 2210); wherein X₁ is G, L or R, wherein X₂ is G, I, or R, wherein X₃ is Y, R, I, G, or A, wherein X₄ is T, S, Y, or V, wherein X₅ is S or Y, wherein X₆ is S, A, I, or R, wherein X₇ is W, A, or S, wherein X₈ is absent or is S, wherein X₉ is absent or is F, W, or Y, wherein X₁₀ is R, S, H, K, or E, wherein X₁₁ is W, H, Y, or F, wherein X₁₂ is Y, V, A, or S, wherein X₁₃ is D or Q, and wherein X₁₄ is L, Y, I, or H;

VAGSNFLFDY (SEQ ID NO: 2670);

GGYTSSWRWYFDL (SEQ ID NO: 2671);

GGYTSSWSRWYFDL (SEQ ID NO: 2672); and

DYGDSFDY (SEQ ID NO: 2673).

[0026] In one aspect, the present disclosure refers to~~various embodiments, provided herein is~~ an isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:

- i. a light chain CDR1 comprising an amino acid sequence $X_1ASQSX_2X_3X_4NLA$ (SEQ ID NO: 2199), wherein X_1 is R or Q, wherein X_2 is V or I, wherein X_3 is N or S, and wherein X_4 is S, H, I, V or A;
 - ii. a light chain CDR2 comprising an amino acid sequence GAX_1X_2RAT (SEQ ID NO: 2200), wherein X_1 is S or Y, and wherein X_2 is T or I; and
 - iii. a light chain CDR3 comprising an amino acid sequence $QX_1X_2X_3X_4X_5X_6PX_7T$ (SEQ ID NO: 2201); wherein X_1 is Q, H or E, wherein X_2 is F or Y, wherein X_3 is K, Y or I, wherein X_4 is N, T, L, I, or M; wherein X_5 is W, F, H or Y, wherein X_6 is absent or P; wherein X_7 is W, N, Y, H or L; and
- d. comprises a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence $X_1X_2X_3MX_4$ (SEQ ID NO: 2202), wherein X_1 is A, R, T or S, wherein X_2 is Y or N, wherein X_3 is A or W, and wherein X_4 is S or N;
 - ii. a heavy chain CDR2 comprising an amino acid sequence $X_1X_2X_3X_4X_5X_6X_7X_8X_9YYX_{10}X_{11}X_{12}VKG$ (SEQ ID NO: 2205), wherein X_1 is T, E, or S, wherein X_2 is absent or is M, V, or I, wherein X_3 is S, R or K, wherein X_4 is G or Q, wherein X_5 is S, D or H, wherein X_6 is G, S L, or A, wherein X_7 is S, G, or R, wherein X_8 is T, S, P or E, wherein X_9 is T or I, wherein X_{10} is A or V, wherein X_{11} is D or E, and wherein X_{12} is S or A; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence $X_1X_2X_3X_4X_5X_6X_7FX_8YYX_9$ (SEQ ID NO: 2203), wherein X_1 is V, E, A or G, wherein X_2 is A, F, Y or G, wherein X_3 is G, S, Y or W, wherein X_4 is S or R, wherein X_5 is absent or is N, wherein X_6 is F, S, Y, or absent, wherein X_7 is L or F or absent, wherein X_8 is D or E, and wherein X_9 is Y, H or S.

[0027] In various ~~embodiment~~examples, the antigen binding protein comprises:

- a. a light chain variable domain comprising:

- i. a light chain CDR1 comprising an amino acid sequence RASQSVNSNLA (SEQ ID NO: 2212);
- ii. a light chain CDR2 comprising an amino acid sequence GASTRAT (SEQ ID NO: 2219);
- iii. a light chain CDR3 comprising an amino acid sequence QQFKNWPPT (SEQ ID NO: 2222); and
- b. a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence AYAMS (SEQ ID NO: 2227);
 - ii. a heavy chain CDR2 comprising an amino acid sequence TSGSGSTTYADSVKG (SEQ ID NO: 2230); and
 - iii. a heavy chain CDR3 comprising an amino acid sequence VAGSNFLFDY (SEQ ID NO: 2670).

[0028] In another aspect, the present disclosure refers to various embodiments, the disclosure provides an isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence QASX₁DIX₂X₃X₄LN (SEQ ID NO: 2204), wherein X₁ is R or Q, wherein X₂ is R, S, N or F, wherein X₃ is K or N, and wherein X₄ is H, Y or D;
 - ii. a light chain CDR2 comprising an amino acid sequence X₁X₂X₃X₄LET (SEQ ID NO: 2206), wherein X₁ is D, G or H, wherein X₂ is A, V or T, wherein X₃ is S, A or Y, and wherein X₄ is T or N;

iii. a light chain CDR3 comprising an amino acid sequence

~~QX₁YX₂X₃X₄PX₅TQX₁YX₂X₃X₄PX₅T~~ (SEQ ID NO: 2207), wherein X₁ is Q or H, wherein X₂ is D, A or G, wherein X₃ is N or K; wherein X₄ is L or I, and wherein X₅ is I or L; and

d. comprises a heavy chain variable domain comprising:

i. a heavy chain CDR1 comprising an amino acid sequence X₁YDIN (SEQ ID NO: 2208), wherein X₁ is R or S;

ii. a heavy chain CDR2 comprising an amino acid sequence

X₁X₂NPX₃X₄GX₅X₆GX₇X₈X₉X₁₀FX₁₁X₁₂ (SEQ ID NO: 2209), wherein X₁ is W or R, wherein X₂ is M or L, wherein X₃ is N, Q, or K, wherein X₄ is S, A, or R, wherein X₅ is N, or Q, wherein X₆ is S, A, or T, wherein X₇ is S, Q, or Y, wherein X₈ is V or T, wherein X₉ is Q or K, wherein X₁₀ is K or N, wherein X₁₁ is R or Q, and wherein X₁₂ is G or D; and

iii. a heavy chain CDR3 comprising an amino acid sequence X₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂FX₁₃X₁₄ (SEQ ID NO: 2210); wherein X₁ is G, L or R, wherein X₂ is G, I, or R, wherein X₃ is Y, R, I, G, or A, wherein X₄ is T, S, Y, or V, wherein X₅ is S or Y, wherein X₆ is S, A, I, or R, wherein X₇ is W, A, or S, wherein X₈ is absent or is S, wherein X₉ is absent or is F, W, or Y, and wherein X₁₀ is R, S, H, K, or E, wherein X₁₁ is W, H, Y, or F, wherein X₁₂ is Y, V, A, or S, wherein X₁₃ is D or Q, and wherein X₁₄ is L, Y, I, or H.

[0029] In various ~~embodiment~~examples, the antigen binding protein comprises:

a. a light chain variable domain comprising:

i. a light chain CDR1 comprising an amino acid sequence QASQDIRKHLN (SEQ ID NO: 2213);

ii. a light chain CDR2 comprising an amino acid sequence DASNLET (SEQ ID NO: 2220); and

iii. a light chain CDR3 comprising an amino acid sequence QHYDNLPIIT (SEQ ID NO: 2223); and

- b. a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence RYDIN (SEQ ID NO: 2228);
 - ii. a heavy chain CDR2 comprising an amino acid sequence WMNPNSGNSSVQKFRG (SEQ ID NO: 2231); and
 - iii. a heavy chain CDR3 comprising an amino acid sequence GGYTSSWRWYFDL (SEQ ID NO: 2671) or GGYTSSWSRWYFDL (SEQ ID NO: 2672).

[0030] In various ~~embodiment~~examples, the disclosure provides an isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TrlGering Receptor Expressed on Myeloid cells 1 (TREM-1) having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a set of CDR sequences selected from:
 - i) SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);
 - ii) SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);
 - iii) SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);
 - iv) SEQ ID NO: 90 (LCDR1), SEQ ID NO: 91 (LCDR2), SEQ ID NO: 92 (LCDR3), SEQ ID NO: 96 (HCDR1), SEQ ID NO: 97 (HCDR2) and SEQ ID NO: 98 (HCDR3);
 - v) SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);

- vi) SEQ ID NO: 130 (LCDR1), SEQ ID NO: 131 (LCDR2), SEQ ID NO: 132 (LCDR3), SEQ ID NO: 136 (HCDR1), SEQ ID NO: 137 (HCDR2) and SEQ ID NO: 138 (HCDR3);
- vii) SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);
- viii) SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3);
- ix) SEQ ID NO: 190 (LCDR1), SEQ ID NO: 191 (LCDR2), SEQ ID NO: 192 (LCDR3), SEQ ID NO: 196 (HCDR1), SEQ ID NO: 197 (HCDR2) and SEQ ID NO: 198 (HCDR3);
- x) SEQ ID NO: 210 (LCDR1), SEQ ID NO: 211 (LCDR2), SEQ ID NO: 212 (LCDR3), SEQ ID NO: 216 (HCDR1), SEQ ID NO: 217 (HCDR2) and SEQ ID NO: 218 (HCDR3);
- xi) SEQ ID NO: 230 (LCDR1), SEQ ID NO: 231 (LCDR2), SEQ ID NO: 232 (LCDR3), SEQ ID NO: 236 (HCDR1), SEQ ID NO: 237 (HCDR2) and SEQ ID NO: 238 (HCDR3);
- xii) SEQ ID NO: 250 (LCDR1), SEQ ID NO: 251 (LCDR2), SEQ ID NO: 252 (LCDR3), SEQ ID NO: 256 (HCDR1), SEQ ID NO: 257 (HCDR2) and SEQ ID NO: 258 (HCDR3);
- xiii) SEQ ID NO: 270 (LCDR1), SEQ ID NO: 271 (LCDR2), SEQ ID NO: 272 (LCDR3), SEQ ID NO: 276 (HCDR1), SEQ ID NO: 277 (HCDR2) and SEQ ID NO: 278 (HCDR3);
- xiv) SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3); or
- xv) SEQ ID NO: 2190 (LCDR1), SEQ ID NO: 2191 (LCDR2), SEQ ID NO: 2192 (LCDR3), SEQ ID NO: 2196 (HCDR1), SEQ ID NO: 2197 (HCDR2) and SEQ ID NO: 2198 (HCDR3).

[0031] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein comprises a set of CDR sequences selected from:

- i) SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);
- ii) SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);
- iii) SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);
- iv) SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);
- v) SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);
- vi) SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3); or
- vii) SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3).

[0032] In various ~~embodiment~~examples, the anti-TREM-1 antigen binding protein comprises a set of CDR sequences selected from: SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) AND SEQ ID NO: 58 (HCDR3; or SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) AND SEQ ID NO: 118 (HCDR3).

[0033] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:

- i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281 301 and 2185;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279, 299 and 2183;
 - iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279 299 and 2183; and
- b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300 and 2184;
 - iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300 and 2184.

[0034] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 121, 161, 181, and 301;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 119, 159, 179, and 299;

- iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 119, 159, 179, and 299; and
- b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 122, 162, 182, and 302;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 40, 60, 80, 120, 160, 180, and 300;
 - iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 40, 60, 80, 120, 160, 180 and 300.

[0035] In various embodiment examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 61 and 121;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 59 and 119;
 - iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 59 and 119; and
- b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 62 and 122;

- ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 60 and 120;
- iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic sequence selected from SEQ ID NOS: 60 and 120.

[0036] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- i) a light chain variable domain set out in SEQ ID NO: 41 and a heavy chain variable domain set out in SEQ ID NO: 42;
- ii) a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62;
- iii) a light chain variable domain set out in SEQ ID NO: 81 and a heavy chain variable domain set out in SEQ ID NO: 82;
- iv) a light chain variable domain set out in SEQ ID NO: 101 and a heavy chain variable domain set out in SEQ ID NO: 102;
- v) a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122;
- vi) a light chain variable domain set out in SEQ ID NO: 161 and a heavy chain variable domain set out in SEQ ID NO: 162;
- vii) a light chain variable domain set out in SEQ ID NO: 181 and a heavy chain variable domain set out in SEQ ID NO: 182;
- viii) a light chain variable domain set out in SEQ ID NO: 201 and a heavy chain variable domain set out in SEQ ID NO: 202;
- x) a light chain variable domain set out in SEQ ID NO: 221 and a heavy chain variable domain set out in SEQ ID NO: 222;
- xi) a light chain variable domain set out in SEQ ID NO: 241 and a heavy chain variable domain set out in SEQ ID NO: 242;
- xii) a light chain variable domain set out in SEQ ID NO: 261 and a heavy chain variable domain set out in SEQ ID NO: 262;

- xiii) a light chain variable domain set out in SEQ ID NO: 281 and a heavy chain variable domain set out in SEQ ID NO: 282;
- xiv) a light chain variable domain set out in SEQ ID NO: 301 and a heavy chain variable domain set out in SEQ ID NO: 302; or
- xv) a light chain variable domain set out in SEQ ID NO: 2185 and a heavy chain variable domain set out in SEQ ID NO: 2186.

[0037] In various embodiment examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- i) a light chain variable domain set out in SEQ ID NO: 41 and a heavy chain variable domain set out in SEQ ID NO: 42;
- ii) a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62;
- iii) a light chain variable domain set out in SEQ ID NO: 81 and a heavy chain variable domain set out in SEQ ID NO: 82;
- iv) a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122;
- v) a light chain variable domain set out in SEQ ID NO: 161 and a heavy chain variable domain set out in SEQ ID NO: 162;
- vi) a light chain variable domain set out in SEQ ID NO: 181 and a heavy chain variable domain set out in SEQ ID NO: 182; or
- vii) a light chain variable domain set out in SEQ ID NO: 301 and a heavy chain variable domain set out in SEQ ID NO: 302.

[0038] In various embodiment examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises: a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62; or a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122.

[0039] In various embodiment examples, the amino acid sequences can be 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to SEQ ID NOs: 42, 62, 82, 102, 122,

142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186, and SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185.

[0040] In various embodimentexamples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186. In various embodimentexamples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence set forth in SEQ ID NO: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185.

[0041] In various embodimentexamples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 122, 162, 182, and 302. In various embodimentexamples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence selected from SEQ ID NO: 41, 61, 81, 121, 161, 181, and 301.

[0042] In various embodimentexamples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence selected from SEQ ID NOS: 62 and 122. In various embodimentexamples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence selected from SEQ ID NO: 61 and 121.

[0043] In various embodimentexamples, one or more heavy chain framework amino acids of the anti- antigen-binding protein are replaced with corresponding amino acid(s) from another human antibody amino acid sequence. In various embodimentexamples, one or more light chain framework amino acids of the antigen-binding protein are replaced with corresponding amino acid(s) from another human antibody amino acid sequence.

[0044] In some instances, a sequence disclosed herein may contain an N-terminal signal sequence useful for recombinant production. Contemplated herein are sequences of anti-TREM-1 antibodies or antigen binding proteins lacking the signal sequences. Exemplary signal sequences include MDMRVPAQLLGLLLLWLRGARC (SEQ ID NO: 2674); MAWALLLLTLLTQGTGSWASYEL (SEQ ID NO: 2675), and nucleic acids encoding such signal sequences.

[0045] In various embodimentexamples, the anti-TREM-1 antigen binding protein further comprises a human light chain constant region attached to said light chain variable region.

[0046] In various embodimentexamples, the heavy chain constant region is selected from heavy chain constant regions of an IgG, IgM, IgA, IgD, IgE, fragments thereof, combinations thereof, and modifications thereof in which one to ten heavy chain framework amino acids are replaced with corresponding amino acid(s) from another human antibody amino acid sequence.

[0047] In various embodimentexamples, the anti-TREM-1 antigen-binding protein described herein inhibits binding of a TREM-1 ligand to TREM-1.

[0048] Also contemplated is an antigen binding protein that competes for binding to a human TREM-1 protein having the sequence of SEQ ID NO: 20 with an anti-TREM-1 antigen binding protein as described herein.

[0049] In various embodimentexamples, the antigen-binding protein is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, a Fab, a F(ab')₂, a Fab₂, a monovalent IgG, an scFv, an scFv-Fc, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody. In various embodimentexamples, the anti-TREM-1 antigen-binding protein is an IgG2 antibody. In various embodimentexamples, the anti-TREM-1 antigen-binding protein is an IgG1 antibody. In various embodimentexamples, the IgG1 antibody is an IgG1z or IgG1z-SEFL2 antibody. In various embodimentexamples, the antigen-binding protein is a monovalent IgG.

[0050] In various embodimentexamples, the antigen-binding protein is a human antibody.

[0051] Also provided is an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain of an anti-TREM-1 antigen binding protein as described herein, an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the light chain of an anti-TREM-1 antigen binding protein as described herein, and an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain and light chain of an anti-TREM-1 antigen binding protein as described herein.

[0052] In various embodimentexamples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region polynucleotide sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280 and 300, and 2184. In various embodimentexamples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region polynucleotide sequence set forth in SEQ ID NO: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279 299 and 2183.

[0053] In various embodimentexamples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region polynucleotide sequence

selected from SEQ ID NOS: 40, 60, 80, 120, 160, 180, and 300. In various ~~embodiment~~examples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region polynucleotide sequence selected from SEQ ID NO: 39, 59, 79, 119, 159, 179, and 299.

[0054] In various ~~embodiment~~examples, the antigen binding protein comprises an amino acid sequence at least 90% identical to a heavy chain variable region polynucleotide sequence selected from SEQ ID NOS: 60 and 120. In various ~~embodiment~~examples, the antigen-binding protein comprises an amino acid sequence at least 90% identical to a light chain variable region polynucleotide sequence selected from SEQ ID NO: 59 and 119.

[0055] Further contemplated is an expression vector comprising the nucleic acid molecules of an anti-TREM-1 antigen binding protein heavy and/or light chain as described herein operably linked to an expression control sequence.

[0056] The disclosure provides a recombinant host cell comprising the nucleic acid molecule comprising a nucleotide sequence encoding the heavy chain of an anti-TREM-1 antigen binding protein or antibody as described herein; or the nucleic acid molecule encoding the light chain or an anti-TREM-1 antibody as described herein; or the nucleic acid molecule encoding a heavy chain and light chain nucleic acid molecule of an anti-TREM-1 antibody as described herein; or the vector comprising the nucleic acid molecules encoding the heavy and/or light chain of an anti-TREM-1 antibody as described herein. In various ~~embodiment~~examples, the host cell is a mammalian cell. In various ~~embodiment~~examples, the host cell is a CHO cell.

[0057] Further provided is a method of using the host cell to produce an antigen-binding protein, comprising culturing the host cell and recovering said antigen-binding protein, and an antigen-binding protein produced by the method.

[0058] Also provided is a sterile pharmaceutical composition comprising the anti-TREM-1 antigen binding protein as described herein and a pharmaceutically acceptable carrier.

[0059] Further contemplated is an antigen binding protein comprising an antigen-binding moiety and one or two IL-10 moieties wherein:

- a. the antigen-binding moiety is an antibody or antibody fragment,
- b. each IL-10 moiety is independently monovalent or bivalent,
- c. each IL-10 moiety is independently selected from one or more human IL-10 muteins having sequences that are 90% identical to SEQ ID NO: 2, and

d. at least one IL-10 moiety is covalently bound to the antigen-binding moiety.

[0060] In various embodimentexamples, at least one IL-10 moiety is fused to a C-terminus of the antigen-binding moiety. In various embodimentexamples, at least one IL-10 moiety is fused to an N-terminus of the antigen-binding moiety. In various embodimentexamples, at least one IL-10 moiety is fused to an N and C terminus of the antigen binding moiety. In various embodimentexamples, the IL-10 moiety is fused at an internal site in the antigen binding moiety. In various embodimentexamples, at least one IL-10 moiety is fused to a heavy and/or light chain of the antigen-binding moiety. In various embodimentexamples, the heavy chain and/or light chain is a modified or engineered heavy chain or light chain.

[0061] Also provided is an antigen binding protein comprising:

(a) a polypeptide sequence having the formula A-L-M or M-L-A, wherein

i) A is an immunoglobulin heavy chain of an IgG antibody that binds to a TREM-1 protein set out in SEQ ID NO: 20,

ii) L is a linker peptide comprising from 4 to 20 amino acids and

iii) M is a mutein of IL-10 having at least 90% sequence identity to wt IL-10 set out in SEQ ID NO: 2; and

(b) an immunoglobulin light chain of an IgG antibody that binds TREM-1 protein set out in SEQ ID NO: 20,

wherein the immunoglobulin heavy chain of (a) and the immunoglobulin light chain of (b) form an IgG antibody moiety that binds TREM-1, wherein the protein comprises one or two molecules of the polypeptide of (a) and one or two molecules of the light chain of (b), optionally wherein only 1 polypeptide of (a) comprises an M moiety.

[0062] In various embodimentexamples, the antigen binding protein reduces the suppression of TNF- α production in myeloid cells, reduces levels of CD8+ T cell stimulation, and/or reduces the level of B cell stimulation compared to wt IL-10.

[0063] In various embodimentexamples of the antigen binding protein:

a. the antigen-binding moiety is an antibody and

b. an IL-10 moiety is fused to each heavy chain of the antibody.

[0064] In various embodimentexamples of the antigen binding protein, each IL-10 moiety is a monomer. In various embodimentexamples the antigen binding protein comprises two different mutein monomers. In various embodimentexamples, the antigen binding protein comprises two of the same mutein monomers.

[0065] In various embodimentexamples of the antigen binding protein: each IL-10 moiety comprises an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 2 and each IL-10 moiety independently comprises at least one mutation selected from a mutation in helical loop AB, helical loop CD, helical loop DE, helix A, helix B, helix C, helix D, helix E and/or helix F.

[0066] In various embodimentexamples of the antigen binding protein, at least one IL-10 moiety comprises at least one mutation in helix A. In various embodimentexamples of the antigen binding protein, at least one IL-10 moiety comprises at least one mutation in helix F. In various embodimentexamples of the antigen binding protein, at least one IL-10 moiety comprises at least one mutation in helical loop AB.

[0067] In various embodimentexamples, the anti-TREM-1/IL-10 mutein antigen binding protein lacks CD8+ T cell stimulation and/or B cell stimulation in a human subject, for example as compared to wt IL-10.

[0068] In various embodimentexamples, the IL-10 mutein reduces the suppression of TNF- α production in myeloid cells, reduces levels of CD8+ T cell stimulation, and/or reduces the level of B cell stimulation compared to wt IL-10.

[0069] In various embodimentexamples, the IL-10 mutein antigen binding protein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, suppresses TNF- α production in myeloid cells. In various embodimentexamples, the IL-10 mutein antigen binding protein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, suppresses TNF- α production in myeloid cells, but still lacks CD8+ T cell and B cell activation.

[0070] In various embodimentexamples, the antigen binding protein with IL-10 mutein fused to the antigen binding partner against cell surface proteins on CD8+ cells and/or B cells enhances levels of CD8+ T cell stimulation and/or levels of B cell stimulation in a human subject.

[0071] In various embodimentexamples of the antigen binding protein, each IL-10 mutein independently comprises a mutation in one or more of residues N10, H14, F15, P20, M22, L23, R24, R27, D28, K34, T35, Q38, M39, K40, D41, Q42, L43, D44, N45, L46, L47, L48, K49, F56, K57, Y59, L60, Q63, E67, Q70, M77, Q79, N82, Q83, D84, P85, D86, I87, A89, H90, S93,

T100, L103, H109, R110, L112, E115, N116, A127, K130, I136, Y137, K138, S141, E142, D144, I145, E151, M154, M156, K157, N160 of SEQ ID NO: 2 and/or an addition of 4-8 amino acids between helix D and helix E.

[0072] In various embodiment examples, each IL-10 mutein independently comprises one or more mutations selected from the group consisting of R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, or I87A of SEQ ID NO: 2, optionally comprising an addition of amino acids between helix D and helix E. In various embodiment examples, each IL-10 mutein independently comprises one or more mutations selected from the group consisting of N10Q, N10I, N10K, R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, I87A, H14Q, F15Y, M22V, K49T, K49S, F56Y, K57N, Y59T, L60Q, Q63E, Q63L, E67C, Q70E, Q70K, M77R, M77V, Q79R, Q79C, D84R, A89P, H90E, H90Q, S93E, S93Q, T100R, L103E, H109D, R110P, R110Q, L112V, E115K, N116D, N116Q, A127M, K130Q, I136C, Y137C, M154V, M156C, K157N, or N160D of SEQ ID NO: 2, optionally comprising an addition of amino acids between helix D and helix E.

[0073] In various embodiment examples, each IL-10 mutein independently comprises one or more mutations selected from the group consisting of R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, or I87A of SEQ ID NO: 2, optionally comprising an addition of six amino acids between helix D and helix E. In various embodiment examples, the amino acids between helix D and helix E are GGGSGG (SEQ ID NO: 2676). In various embodiment examples, each IL-10 mutein independently comprises one or more mutations selected from the group consisting of N10Q, N10I, N10K, R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, I87A, H14Q, F15Y, M22V, K49T, K49S, F56Y, K57N, Y59T, L60Q, Q63E, Q63L, E67C, Q70E, Q70K, M77R, M77V, Q79R, Q79C, D84R, A89P, H90E, H90Q, S93E, S93Q, T100R, L103E, H109D, R110P, R110Q, L112V, E115K, N116D, N116Q, A127M, K130Q, I136C, Y137C, M154V, M156C, K157N, or N160D of SEQ ID NO: 2, optionally comprising an addition of six amino acids between helix D and helix E. In various embodiment examples, the amino acids between helix D and helix E are GGGSGG (SEQ ID NO: 2676).

[0074] In various embodiment examples of the antigen binding protein, each IL-10 mutein is at least 95% identical to the amino acid sequence set forth in SEQ ID NO: 2. In various embodiment examples, the amino acid sequence of the IL-10 mutein is set out in SEQ ID NO: 3-10. In various embodiment examples, the amino acid sequence of the IL-10 mutein is set out in SEQ ID NO: 3-10 and SEQ ID NOS: 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170, 2172, 2174, 2176, 2178, 2180, 2182, 2360, 2362, 2364, 2366, 2368,

2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436, 2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2538, 2540 and 2777-2791.

[0075] In various embodimentexamples, the antigen binding protein comprises at least one linker fused to at least one C-terminus of the antigen-binding moiety and an IL-10 moiety is covalently bound to the C-terminus of each linker. In various embodimentexamples, the linker is between 4 and 18 amino acids long. In various embodimentexamples, the linker is six amino acids long. In various embodimentexamples, the linker is a 3-mer, 4-mer, 5-mer, 6-mer, 7-mer or 8-mer peptide. In various embodimentexamples, the linker comprises GS residues.

[0076] In various embodimentexamples, the antigen binding protein comprises a “buried” IL-10 mutein. In various embodimentexamples, the antigen binding protein comprises: (a) a Fab portion of an anti- TREM1 binding moiety, (b) at least one G4 linker fused to C-terminus of the Fab portion of the TREM1-binding moiety, (c) an IL-10 moiety is covalently bound to the C-terminus of each linker; another G4 linker is fused to the C-terminus of the IL10 moiety; the Fc region is covalently attached to the C-terminus of this second G4 linker. Additional linkers contemplated are described further in the Detailed Description.

[0077] In various embodimentexamples, the antigen binding moiety in the antigen binding protein further comprises a human heavy chain constant region attached to said heavy chain variable region of the antibody portion of the antigen binding protein. In various embodimentexamples, the antigen binding protein further comprises a human light chain constant region attached to said light chain variable region of the antibody portion of the antigen binding protein.

[0078] In various embodimentexamples of the antigen binding protein, the antigen-binding moiety is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, a Fab, a F(ab')₂, a Fab₂, a monovalent IgG, an scFv, an scFv-Fc, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody. In various embodimentexamples, the antigen-binding moiety is an IgG. In various embodimentexamples, the antigen-binding moiety is an IgG2 antibody. In various embodimentexamples, the antigen-binding moiety is an IgG1 antibody. In various embodimentexamples of the antigen binding protein, the antibody is an IgG1z or IgG1z-SEFL2 antibody. In various embodimentexamples, the antigen-binding moiety is a monovalent IgG. In various embodimentexamples, the heavy chain constant

region of the antigen-binding moiety is selected from heavy chain constant regions of an IgG, IgM, IgA, IgD, IgE, fragments thereof, combinations thereof, and modifications thereof in which one to ten heavy chain framework amino acids are replaced with corresponding amino acid(s) from another human antibody constant region.

[0079] In various ~~embodiment~~examples of the antigen binding protein, the antigen-binding moiety binds to human PD-1 having the amino acid sequence set forth in SEQ ID NO: 22. In various ~~embodiment~~examples, the antigen-binding moiety binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20. In various ~~embodiment~~examples, the antigen-binding moiety binds to the human TREM-1 with a binding affinity of at least 10^{-8} M. In various ~~embodiment~~examples, the antigen binding moiety binds its antigen with a binding affinity of at least 10^{-8} M to 10^{-15} M or 10^{-8} M to 10^{-12} M, or 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M, 10^{-13} M, 10^{-14} M, or 10^{-15} M.

[0080] In various ~~embodiment~~examples of the antigen binding protein, the anti-TREM-1 antigen binding moiety comprises:

- a. a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 30, 50, 70, 90, 110, 130, 150, 170, 190, 210, 230, 250, 270, 290 and 2190;
 - ii. a light chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NOS: 31, 51, 71, 91, 111, 131, 151, 171, 191, 211, 231, 251, 271, 291 and 2191;
 - iii. a light chain CDR3 sequence comprising an amino acid sequence selected from SEQ ID NOS: 32, 52, 72, 92, 112, 132, 152, 172, 192, 212, 232, 252, 272, 292 and 2192; and
- b. comprises a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 36, 56, 76, 96, 116, 136, 156, 176, 196, 216, 236, 256, 276, 296 and 2196;
 - ii. a heavy chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NOS: 37, 57, 77, 97, 117, 137, 157, 177, 197, 217, 237, 257, 277, 297 and 2197; and
 - iii. a heavy chain CDR3 sequence comprising an amino acid sequence selected from SEQ ID NOS: 38, 58, 78, 98, 118, 138, 158, 178, 198, 218, 238, 258, 278, 298 and 2198.

[0081] In various ~~embodiment~~examples of the antigen binding protein, the anti-TREM-1 antigen binding moiety comprises:

- a. the light chain CDR1 sequence is set out in SEQ ID NO: 30, 50, 70, 110, 150, 170, or 290;

- b. the light chain CDR2 sequence is set out in SEQ ID NO: 31, 51, 71, 111, 151, 171, or 291;
- c. the light chain CDR3 sequence is set out in SEQ ID NO: 32, 52, 72, 112, 152, 172, or 292
- d. the heavy chain CDR1 sequence is set out in SEQ ID NO: 36, 56, 76, 116, 156, 176, or 296 ;
- e. the heavy chain CDR2 sequence is set out in SEQ ID NO: 37, 57, 77, 117, 157, 177, or 297; and
- f. the heavy chain CDR3 sequence is set out in SEQ ID NO: 38, 58, 78, 118, 158, 178, or 298.

[0082] In various embodiment examples of the antigen binding protein, the anti-TREM-1 antigen binding moiety comprises:

- a. the light chain CDR1 sequence is set out in SEQ ID NO: 50 or 110;
- b. the light chain CDR2 sequence is set out in SEQ ID NO: 51 or 111;
- c. the light chain CDR3 sequence is set out in SEQ ID NO: 52 or 112;
- d. the heavy chain CDR1 sequence is set out in SEQ ID NO: 56 or 116;
- e. the heavy chain CDR2 sequence is set out in SEQ ID NO: 57 or 117; and
- f. the heavy chain CDR3 sequence is set out in SEQ ID NOS: 58 or 118.

[0083] In various embodiment examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises a set of CDR sequences selected from:

- i) SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);
- ii) SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);
- iii) SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);

- iv) SEQ ID NO: 90 (LCDR1), SEQ ID NO: 91 (LCDR2), SEQ ID NO: 92 (LCDR3), SEQ ID NO: 96 (HCDR1), SEQ ID NO: 97 (HCDR2) and SEQ ID NO: 98 (HCDR3);
- v) SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);
- vi) SEQ ID NO: 130 (LCDR1), SEQ ID NO: 131 (LCDR2), SEQ ID NO: 132 (LCDR3), SEQ ID NO: 136 (HCDR1), SEQ ID NO: 137 (HCDR2) and SEQ ID NO: 138 (HCDR3);
- vii) SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);
- viii) SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3);
- ix) SEQ ID NO: 190 (LCDR1), SEQ ID NO: 191 (LCDR2), SEQ ID NO: 192 (LCDR3), SEQ ID NO: 196 (HCDR1), SEQ ID NO: 197 (HCDR2) and SEQ ID NO: 198 (HCDR3);
- x) SEQ ID NO: 210 (LCDR1), SEQ ID NO: 211 (LCDR2), SEQ ID NO: 212 (LCDR3), SEQ ID NO: 216 (HCDR1), SEQ ID NO: 217 (HCDR2) and SEQ ID NO: 218 (HCDR3);
- xi) SEQ ID NO: 230 (LCDR1), SEQ ID NO: 231 (LCDR2), SEQ ID NO: 232 (LCDR3), SEQ ID NO: 236 (HCDR1), SEQ ID NO: 237 (HCDR2) and SEQ ID NO: 238 (HCDR3);
- xii) SEQ ID NO: 250 (LCDR1), SEQ ID NO: 251 (LCDR2), SEQ ID NO: 252 (LCDR3), SEQ ID NO: 256 (HCDR1), SEQ ID NO: 257 (HCDR2) and SEQ ID NO: 258 (HCDR3);
- xiii) SEQ ID NO: 270 (LCDR1), SEQ ID NO: 271 (LCDR2), SEQ ID NO: 272 (LCDR3), SEQ ID NO: 276 (HCDR1), SEQ ID NO: 277 (HCDR2) and SEQ ID NO: 278 (HCDR3);

- xiv) SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3); and
- xv) SEQ ID NO: 2190 (LCDR1), SEQ ID NO: 2191 (LCDR2), SEQ ID NO: 2192 (LCDR3), SEQ ID NO: 2196 (HCDR1), SEQ ID NO: 2197 (HCDR2) and SEQ ID NO: 2198 (HCDR3).

[0084] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises a set of CDR sequences selected from:

- i) SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);
- ii) SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);
- iii) SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);
- iv) SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);
- v) SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);
- vi) SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3); and
- vii) SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3).

[0085] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises a set of CDR sequences selected from: SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3),

SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3); and SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3).

[0086] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:

i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185;

ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279 299 and 2183;

iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279, 299 and 2183; and

b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:

i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186;

ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300 and 2184;

iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280 300 and 2184.

[0087] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:

- i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 121, 161, 181, and 301;
- ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 119, 159, 179, and 299;
- iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 119, 159, 179, and 299; and

b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:

- i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 122, 162, 182, and 302;
- ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 40, 60, 80, 120, 160, 180, and 300;
- iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 40, 60, 80, 120, 160, 180, and 300.

[0088] In various ~~embodiment~~examples of the antigen binding protein, the anti-TREM-1 antigen-binding moiety comprises:

a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:

- i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 61 and 121;
- ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to a nucleic acid sequence selected from SEQ ID NOS: 59 and 119;

- iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 59 and 119; and
- b. a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:
 - i. a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 62 and 122;
 - ii. a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 60 and 120;
 - iii. a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 60 and 120.

[0089] In various embodiment examples, the amino acid sequences can be 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185 and SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186.

[0090] In various embodiment examples of the antigen binding protein, the antigen binding moiety comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186.

[0091] In various embodiment examples of the antigen binding protein, the antigen-binding moiety comprises an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185.

[0092] In various embodiment examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- i) a light chain variable domain set out in SEQ ID NO: 41 and a heavy chain variable domain set out in SEQ ID NO: 42;
- ii) a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62;

- iii) a light chain variable domain set out in SEQ ID NO: 81 and a heavy chain variable domain set out in SEQ ID NO: 82;
- iv) a light chain variable domain set out in SEQ ID NO: 101 and a heavy chain variable domain set out in SEQ ID NO: 102;
- v) a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122;
- vi) a light chain variable domain set out in SEQ ID NO: 141 and a heavy chain variable domain set out in SEQ ID NO: 142;
- vii) a light chain variable domain set out in SEQ ID NO: 161 and a heavy chain variable domain set out in SEQ ID NO: 162;
- viii) a light chain variable domain set out in SEQ ID NO: 181 and a heavy chain variable domain set out in SEQ ID NO: 182;
- ix) a light chain variable domain set out in SEQ ID NO: 201 and a heavy chain variable domain set out in SEQ ID NO: 202;
- x) a light chain variable domain set out in SEQ ID NO: 221 and a heavy chain variable domain set out in SEQ ID NO: 222;
- xi) a light chain variable domain set out in SEQ ID NO: 241 and a heavy chain variable domain set out in SEQ ID NO: 242;
- xii) a light chain variable domain set out in SEQ ID NO: 261 and a heavy chain variable domain set out in SEQ ID NO: 262;
- xiii) a light chain variable domain set out in SEQ ID NO: 281 and a heavy chain variable domain set out in SEQ ID NO: 282;
- xiv) a light chain variable domain set out in SEQ ID NO: 301 and a heavy chain variable domain set out in SEQ ID NO: 302; or
- xv) a light chain variable domain set out in SEQ ID NO: 2185 and a heavy chain variable domain set out in SEQ ID NO: 2186.

[0093] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of an antigen binding protein comprises:

- i) a light chain variable domain set out in SEQ ID NO: 41 and a heavy chain variable domain set out in SEQ ID NO: 42;

- ii) a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62;
- iii) a light chain variable domain set out in SEQ ID NO: 81 and a heavy chain variable domain set out in SEQ ID NO: 82;
- iv) a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122;
- v) a light chain variable domain set out in SEQ ID NO: 161 and a heavy chain variable domain set out in SEQ ID NO: 162;
- vi) a light chain variable domain set out in SEQ ID NO: 181 and a heavy chain variable domain set out in SEQ ID NO: 182; or
- vii) a light chain variable domain set out in SEQ ID NO: 301 and a heavy chain variable domain set out in SEQ ID NO: 302.

[0094] In various ~~embodiment~~examples, the anti-TREM-1 antigen-binding protein or anti-TREM1 antigen-binding portion of a antigen binding protein comprises: a light chain variable domain set out in SEQ ID NO: 61 and a heavy chain variable domain set out in SEQ ID NO: 62; or a light chain variable domain set out in SEQ ID NO: 121 and a heavy chain variable domain set out in SEQ ID NO: 122.

[0095] In various ~~embodiment~~examples, the antigen binding protein has a light chain amino acid sequence set out in any one of SEQ ID NOS: 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.

[0096] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a light chain amino acid sequence set out in any one of SEQ ID NOS: 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605.

[0097] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a light chain amino acid sequence set out in any one of SEQ ID NO: 2233, 2235, 2237, 2239, 2241, 2243, 2245, 2247, 2249, 2251, 2253, 2255, 2257, 2259, 2261, 2263, 2265, 2267, 2269, 2271, 2273, 2275, 2277, 2279, 2281, 2283, 2285, 2287, 2289, 2291, 2293, 2295, 2297, 2299, 2301, 2303, 2305, 2307, 2309, 2311, 2313, 2315, 2317, 2319, 2321, 2323, 2325, 2327, 2329, 2331, 2333, 2335, 2337, 2339, 2341, 2343, 2345, 2347, 2349, 2351, 2353, 2355, and 2357.

[0098] In various ~~embodiment~~examples, the antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085.

[0099] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 1883, 1885, 1887, 1889, 1891, 1893, 1895, 1897, 1899, 1901, 1903, 1905, 1907, 1909, 1911, 1913, 1915, 1917, 1919, 1921, 1923, 1925, 1927, 1929, 1931, 1933, 1935, 1937, 1939, 1941, 1943, 1945, 1947, 1949, 1951, 1953, 1955, 1957, 1959, 1961, 1963, 1965, 1967, 1969, 1971, 1973, 1975, 1977, 1979, 1981, 1983, 1985, 1987, 1989, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, and 2007.

[0100] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2011, 2013, 2015, 2017, 2019, 2021, 2026, 2025, 2027, 2029, 2031, 2033, 2035, 2037, 2039, 2041, 2043, 2045, 2047, 2049, 2051, 2053, 2055, 2057, 2059, 2061, 2063, 2065, 2067, 2069, 2071, 2073, 2075, 2077, 2079, 2081, 2083, 2085, 2087, 2089, 2091, 2093, 2095, 2097, 2099, 2101, 2103, 2105, 2107, 2109, 2111, 2113, 2115, 2117, 2119, 2121, 2123, 2125, 2127, 2129, 2131, 2133, and 2135.

[0101] In various ~~embodiment~~examples, the antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2726-2776.

[0102] In various ~~embodiment~~examples, the antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957,

959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085 and a corresponding light chain amino acid sequence set out in SEQ ID NOS: 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.

[0103] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 1883, 1885, 1887, 1889, 1891, 1893, 1895, 1897, 1899, 1901, 1903, 1905, 1907, 1909, 1911, 1913, 1915, 1917, 1919, 1921, 1923, 1925, 1927, 1929, 1931, 1933, 1935, 1937, 1939, 1941, 1943, 1945, 1947, 1949, 1951, 1953, 1955, 1957, 1959, 1961, 1963, 1965, 1967, 1969, 1971, 1973, 1975, 1977, 1979, 1981, 1983, 1985, 1987, 1989, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, and 2007 and a corresponding light chain amino acid sequence set out in SEQ ID NOS: 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, and 2605.

[0104] In various ~~embodiment~~examples, the TREM-1 antibody or antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2011, 2013, 2015, 2017, 2019, 2021, 2026, 2025, 2027, 2029, 2031, 2033, 2035, 2037, 2039, 2041, 2043, 2045, 2047, 2049, 2051, 2053, 2055, 2057, 2059, 2061, 2063, 2065, 2067, 2069, 2071, 2073, 2075, 2077, 2079, 2081, 2083, 2085, 2087, 2089, 2091, 2093, 2095, 2097, 2099, 2101, 2103, 2105, 2107, 2109, 2111, 2113, 2115, 2117, 2119, 2121, 2123, 2125, 2127, 2129, 2131, 2133, and 2135 and a corresponding light chain amino acid sequence set out in SEQ ID NO: 2233, 2235, 2237, 2239, 2241, 2243, 2245, 2247, 2249, 2251, 2253, 2255, 2257, 2259, 2261, 2263, 2265, 2267, 2269, 2271, 2273, 2275, 2277, 2279, 2281, 2283, 2285, 2287, 2289, 2291, 2293, 2295, 2297, 2299,

2301, 2303, 2305, 2307, 2309, 2311, 2313, 2315, 2317, 2319, 2321, 2323, 2325, 2327, 2329, 2331, 2333, 2335, 2337, 2339, 2341, 2343, 2345, 2347, 2349, 2351, 2353, 2355, and 2357.

[0105] In various ~~embodiment~~examples, the antigen binding protein has the heavy and light chain pairs as set out in Table 10, Table 11, Table 13A, or Table 13B, or utilizes the heavy chain antigen binding protein set out in Table 16, Table 17 or Table 22.

[0106] Nucleic acid sequences of certain antigen binding protein heavy and light chains are set out in SEQ ID NOS: 303 to 526 (bivalent) and SEQ ID NOS: 527 to 862 (monovalent). Nucleic acid sequences of TREM-1 variant antibody heavy chain variable regions are set out in SEQ ID NOS: 1884, 1886, 1888, 1890, 1892, 1894, 1896, 1898, 1900, 1902, 1904, 1906, 1908, 1910, 1912, 1914, 1916, 1918, 1920, 1922, 1924, 1926, 1928, 1930, 1932, 1934, 1936, 1938, 1940, 1942, 1944, 1946, 1948, 1950, 1952, 1954, 1956, 1958, 1960, 1962, 1964, 1966, 1968, 1970, 1972, 1974, 1976, 1978, 1980, 1982, 1984, 1986, 1988, 1990, 1992, 1994, 1996, 1998, 2000, 2002, 2004, 2006, and 2008, and also set out in SEQ ID NOS: 2012, 2014, 2016, 2018, 2020, 2022, 2024, 2026, 2028, 2030, 2032, 2034, 2036, 2038, 2040, 2042, 2044, 2046, 2048, 2050, 2052, 2054, 2056, 2058, 2060, 2062, 2064, 2066, 2068, 2070, 2072, 2074, 2076, 2078, 2080, 2082, 2084, 2086, 2088, 2090, 2092, 2094, 2096, 2098, 2100, 2102, 2104, 2106, 2108, 2110, 2112, 2114, 2116, 2118, 2120, 2122, 2124, 2126, 2128, 2130, 2132, 2134, and 2136; and TREM-1 variant antibody light chain variable regions nucleotide sequences are set out in SEQ ID NO: 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, and also set out in SEQ ID NO: 2234, 2236, 2238, 2240, 2242, 2244, 2246, 2248, 2250, 2252, 2254, 2256, 2258, 2260, 2262, 2264, 2266, 2268, 2270, 2272, 2274, 2276, 2278, 2280, 2282, 2284, 2286, 2288, 2290, 2292, 2294, 2296, 2298, 2300, 2302, 2304, 2306, 2308, 2310, 2312, 2314, 2316, 2318, 2320, 2322, 2324, 2326, 2328, 2330, 2332, 2334, 2336, 2338, 2340, 2342, 2344, 2346, 2348, 2350, 2352, 2354, 2356, and 2358.

[0107] In various ~~embodiment~~examples of the antigen binding proteins, one or more heavy chain framework amino acids of the anti- antigen-binding protein are replaced with corresponding amino acid(s) from another human antibody amino acid sequence. In various ~~embodiment~~examples, one or more light chain framework amino acids of the antigen-binding protein are replaced with corresponding amino acid(s) from another human antibody amino acid sequence.

[0108] In various ~~embodiment~~examples, the anti-TREM-1 antigen binding protein further comprises a human light chain constant region attached to said light chain variable region.

[0109] In various ~~embodiment~~examples of the antigen binding protein: the antigen binding protein comprises two light chains and two heavy chains: each heavy chain comprises an IL-10 moiety attached at the C-terminus of the heavy chain; each heavy-chain-IL-10 moiety antigen binding protein comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085; and each light chain comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS: 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.

[0110] In various ~~embodiment~~examples, provided herein are variants of the TREM-1 antibody heavy chain and/or light chain variable regions. TREM-1 antibody heavy chain variable region variant sequences are set out in SEQ ID NO: 1883, 1885, 1887, 1889, 1891, 1893, 1895, 1897, 1899, 1901, 1903, 1905, 1907, 1909, 1911, 1913, 1915, 1917, 1919, 1921, 1923, 1925, 1927, 1929, 1931, 1933, 1935, 1937, 1939, 1941, 1943, 1945, 1947, 1949, 1951, 1953, 1955, 1957, 1959, 1961, 1963, 1965, 1967, 1969, 1971, 1973, 1975, 1977, 1979, 1981, 1983, 1985, 1987, 1989, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007, 2011, 2013, 2015, 2017, 2019, 2021, 2026, 2025, 2027, 2029, 2031, 2033, 2035, 2037, 2039, 2041, 2043, 2045, 2047, 2049, 2051, 2053, 2055, 2057, 2059, 2061, 2063, 2065, 2067, 2069, 2071, 2073, 2075, 2077, 2079, 2081, 2083, 2085, 2087, 2089, 2091, 2093, 2095, 2097, 2099, 2101, 2103, 2105, 2107, 2109, 2111, 2113, 2115, 2117, 2119, 2121, 2123, 2125, 2127, 2129, 2131, 2133, 2135, 2726-2776 and Table 10, Table 11, Table 13A, Table 13B and Table 22.

[0111] TREM-1 antibody light chain variable region variant sequences are set out in SEQ ID NOS: 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2233, 2235, 2237, 2239, 2241, 2243, 2245, 2247, 2249, 2251, 2253, 2255, 2257, 2259, 2261, 2263, 2265, 2267, 2269, 2271, 2273, 2275, 2277, 2279, 2281, 2283, 2285, 2287, 2289, 2291, 2293, 2295, 2297, 2299, 2301, 2303, 2305, 2307, 2309, 2311, 2313, 2315, 2317, 2319, 2321, 2323, 2325, 2327, 2329, 2331, 2333, 2335, 2337, 2339, 2341, 2343, 2345, 2347, 2349, 2351, 2353, 2355, 2357, Table 10 and Table 11. It is contemplated that a TREM-1-IL-10 antigen binding protein comprises a TREM-1 antibody variant heavy chain and/or light chain sequence as disclosed herein.

[0112] In various ~~embodiment~~examples, the antigen binding protein may be monovalent. In various ~~embodiment~~examples the heavy-chain-IL-10 moiety antigen binding protein comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS:

1087, 1090, 1093, 1096, 1105, 1108, 1111, 1114, 1117, 1123, 1126, 1129, 1132, 1138, 1141, 1147, 1150, 1153, 1156, 1159, 1162, 1165, 1168, 1171, 1174, 1177, 1180, 1183, 1186, 1189, 1192, 1195, 1198, 1201, 1204, 1207, 1210, 1213, 1216, 1219, 1222, 1225, 1228, 1231, 1237, 1240, 1243, 1246, 1252, 1255, 1258, 1261, 1264, 1267, 1270, 1273, 1276, 1279, 1285, 1288, 1294, 1297, 1300, 1303, 1309, 1312, 1315, 1318, 1321, 1324, 1333, 1336, 1342, 1345, 1348, 1351, 1354, 1357, 1360, 1363, 1366, 1369, 1372, 1375, 1378, 1381, 1384, 1387, 1390, 1393, 1396, 1399, 1402, 1408, 1411, 1414, 1417, and 1420. In various ~~embodiment~~examples, the light-chain comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS: 1088, 1091, 1094, 1097, 1106, 1109, 1112, 1115, 1118, 1124, 1127, 1130, 1133, 1139, 1142, 1148, 1151, 1154, 1157, 1160, 1163, 1166, 1169, 1172, 1175, 1178, 1181, 1184, 1187, 1190, 1193, 1196, 1199, 1202, 1205, 1208, 1211, 1214, 1217, 1220, 1223, 1226, 1229, 1232, 1238, 1241, 1244, 1247, 1253, 1256, 1259, 1262, 1265, 1268, 1271, 1274, 1277, 1280, 1286, 1289, 1295, 1298, 1301, 1304, 1310, 1313, 1316, 1319, 1322, 1325, 1334, 1337, 1343, 1346, 1349, 1352, 1355, 1358, 1361, 1364, 1367, 1370, 1373, 1376, 1379, 1382, 1385, 1388, 1391, 1394, 1397, 1400, 1403, 1409, 1412, 1415, 1418 and 1421. In various ~~embodiment~~examples, the monovalent antigen binding protein further comprises an Fc region, e.g., as set out in SEQ ID NO: 1089, 1092, 1095, 1098, 1107, 1110, 1113, 1116, 1119, 1125, 1128, 1131, 1134, 1140, 1143, 1149, 1152, 1155, 1158, 1161, 1164, 1167, 1170, 1173, 1176, 1179, 1182, 1185, 1188, 1191, 1194, 1197, 1200, 1203, 1206, 1209, 1212, 1215, 1218, 1221, 1224, 1227, 1230, 1233, 1239, 1242,

1245, 1248, 1254, 1257, 1260, 1263, 1266, 1269, 1272, 1275, 1278, 1281, 1287, 1290, 1296, 1299, 1302, 1305, 1311, 1314, 1317, 1320, 1323, 1326, 1335, 1338, 1344, 1347, 1350, 1353, 1356, 1359, 1362, 1365, 1368, 1371, 1374, 1377, 1380, 1383, 1386, 1389, 1392, 1395, 1398, 1401, 1404, 1410, 1413, 1416, 1419 and 1422. The monovalent antigen binding proteins, and Fc region may be assembled or matched as set out in Table 13B.

[0113] In various ~~embodiment~~examples of the antigen binding protein: the antigen binding protein comprises one or two light chains and one or two heavy chains: each heavy chain comprises an IL-10 moiety attached at the C-terminus of the heavy chain; each heavy-chain-IL-10 moiety antigen binding protein comprises an amino acid sequence at least 90% identical to a sequence selected from: SEQ ID NO: 2137, 2139, 2141, 2143, 2145, 2147, 2149, 2151, 2153, 2155, 2157, 2159, 2161, 2163, 2165, 2167, 2169, 2171, 2173, 2175, 2177, 2179, 2181, 2359, 2361, 2363, 2365, 2367, 2369, 2371, 2373, 2375, 2377, 2379, 2381, 2383, 2385, 2387, 2389, 2391, 2393, 2395, 2397, 2399, 2401, 2403, 2405, 2407, 2409, 2411, 2143, 2415, 2417, 2419, 2421, 2423, 2425, 2427, 2429, 2431, 2433, 2435, 2437, 2439, 2441, 2443, 2445, 2447, 2449, 2451, 2453, 2455, 2457, 2459, 2461, 2463, 2465, 2467, 2469, 2471, 2473, 2475, 2477, 2479, 2481, 2483, 2485, 2487, 2489, 2491, 2493, 2495, 2497, 2498, 2499, 2501, 2503, 2505, 2507, 2509, 2511, 2513, 2515, 2517, 2519, 2521, 2523, 2525, 2527, 2529, 2531, 2533, 2535, 2537, 2539, and 2726-2776, and as set out in Table 16 or Table 17 or Table 21 or Table 22.

[0114] In various ~~embodiment~~examples, the antigen binding protein comprises an amino acid sequence selected from: SEQ ID NOS: 2137, 2139, 2141, 2143, 2145, 2147, 2149, 2151, 2153, 2155, 2157, 2159, 2161, 2163, 2165, 2167, 2169, 2171, 2173, 2175, 2177, 2179, 2181, 2359, 2361, 2363, 2365, 2367, 2369, 2371, 2373, 2375, 2377, 2379, 2381, 2383, 2385, 2387, 2389, 2391, 2393, 2395, 2397, 2399, 2401, 2403, 2405, 2407, 2409, 2411, 2143, 2415, 2417, 2419, 2421, 2423, 2425, 2427, 2429, 2431, 2433, 2435, 2437, 2439, 2441, 2443, 2445, 2447, 2449, 2451, 2453, 2455, 2457, 2459, 2461, 2463, 2465, 2467, 2469, 2471, 2473, 2475, 2477, 2479, 2481, 2483, 2485, 2487, 2489, 2491, 2493, 2495, 2497, 2498, 2499, 2501, 2503, 2505, 2507, 2509, 2511, 2513, 2515, 2517, 2519, 2521, 2523, 2525, 2527, 2529, 2531, 2533, 2535, 2537, and 2539. In various ~~embodiment~~examples, the heavy chain portion of the antigen binding protein pairs with a corresponding light chain clone, e.g., antibody 61B12 (SEQ ID NO: 105, but lacking the signal sequence or SEQ ID NO: 2552, TREM1_61B12.001_hulgGz SEFL2 light chain, or SEQ ID NO: 1042, 1044, 1046, 1048, 1052, 1054), or as set out in SEQ ID NO: 2233 to 2358, Table 10 or Table 11.

[0115] In various embodimentexamples, the antigen binding protein has a heavy chain amino acid sequence at least 90% identical to a sequence set out in any one of SEQ ID NOS: 2726-2776. In various embodimentexamples, the antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2726-2776. In various embodimentexamples, the antigen binding protein has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2727-2732. In various embodimentexamples, the heavy chain pairs with a corresponding light chain clone, e.g., SEQ ID NO: 976 or SEQ ID NO: 2554 for clone 63F8.001 (but lacking the signal sequence), and SEQ ID NO: 992 or SEQ ID NO: 2555 for 64D7.001 (but lacking the signal sequence). In various embodimentexamples, the antigen binding protein comprises the heavy chain amino acid sequence of SEQ ID NO: 2727 or 2728, and the light chain amino acid sequence set out in SEQ ID NO: 976 or SEQ ID NO: 2554, or other light chain sequence for clone 63F8 or 63F8.001 as described herein. In various embodimentexamples, the antigen binding protein comprises the heavy chain amino acid sequence of SEQ ID NO: 2729, 2730, 2731 or 2732, and the light chain amino acid sequence set out in and SEQ ID NO: 992 or SEQ ID NO: 2555 or other light chain sequence for 64D7 or 64D7.001 as described herein.

[0116] In various embodimentexamples of the antigen binding protein, the antigen-binding moiety inhibits TREM-1 ligand(s) binding to TREM-1.

[0117] In various embodimentexamples, the antigen binding protein comprises an antigen-binding moiety and one or two IL-10 mutein moieties wherein:

- a. the antigen-binding moiety is an antibody or antibody fragment,
- b. each IL-10 moiety is independently monovalent or bivalent,
- c. each IL-10 moiety is independently selected from and one or more human IL-10 muteins having sequences that are 90% identical to SEQ ID NO: 2,
- d. at least one IL-10 moiety is covalently bound to the antigen-binding moiety, and
- e. the antigen-binding moiety competes for binding to a human TREM-1 protein with the anti-TREM-1 antigen binding moiety described herein.

[0118] In various embodimentexamples of the antigen binding protein, the antigen-binding moiety is a human antibody.

[0119] Also provided is an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain region of the antigen binding protein of as described herein, an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the light chain

region of the antigen binding protein of as described herein, and an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain region of the antigen binding protein and further comprising a nucleotide sequence that encodes the light chain region of the antigen binding protein as described herein.

[0120] The disclosure provides an expression vector or vectors comprising the nucleic acid molecule or molecules encoding a antigen binding protein as described herein operably linked to an expression control sequence.

[0121] Also contemplated is a recombinant host cell comprising the nucleic acid molecule comprising an antigen binding protein as described herein, or the vector comprising said nucleic acid. In various embodimentexamples, the host cell is a mammalian cell. In various embodimentexamples, the host cell is a CHO cell. The disclosure provides a method of using the host cell described herein to produce an antigen binding protein, comprising culturing the host cell and recovering said antibody, and provides an antigen binding protein produced by the method.

[0122] The disclosure contemplates a pharmaceutical composition comprising the antigen binding protein as described herein and a pharmaceutically acceptable carrier. Also provided is a pharmaceutical composition comprising an IL-10 mutein of this disclosure. Further provided is a pharmaceutical composition comprising an anti-TREM-1 antibody or antibody fragment of this disclosure. It is contemplated that the pharmaceutical compositions are sterile pharmaceutical compositions.

[0123] In one aspectexample, the disclosure provides a method of treating an inflammatory disease in a subject in a need thereof comprising administering an IL-10 mutein as described herein or a composition comprising an IL-10 mutein.

[0124] In a related aspectexample, the disclosure provides a method of treating an inflammatory disease in a subject in a need thereof comprising administering an anti-TREM-1 antigen-binding protein as described herein or a composition comprising an anti-TREM-1 antigen binding protein as described herein. In various embodimentexamples, the method further comprises administering an anti-IL-10 mutein as described herein in combination with an anti-TREM-1 antigen binding protein. In various embodimentexamples, the anti-TREM-1 antigen-binding protein and the IL-10 mutein are administered in the same composition or in different compositions.

[0125] Also provided is a method of treating an inflammatory disease in a subject in a need thereof comprising administering a antigen binding protein as described herein or a composition of comprising an antigen binding protein as described herein. In various embodimentexamples,

provided is a method of treating an inflammatory disease in a subject in a need thereof comprising administering an anti-TREM-1/IL-10 mutein antigen binding protein as described herein or a composition of comprising said antigen binding protein.

[0126] In various embodimentexamples, the inflammatory disease is selected from the group consisting of inflammatory bowel disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome, rheumatoid arthritis, psoriasis, psoriatic arthritis, or cytokine release syndrome (CRS). In one embodimentexample, the inflammatory disease is inflammatory bowel disease. In one embodimentexample, the inflammatory disease is ulcerative colitis. In one embodimentexample, the inflammatory disease is Crohn's disease. In one embodimentexample, the inflammatory disease is irritable bowel syndrome. In one embodimentexample, the inflammatory disease is rheumatoid arthritis. In one embodimentexample, the inflammatory disease is psoriasis. In one embodimentexample, the inflammatory disease is psoriatic arthritis. In one embodimentexample, the inflammatory disease is cytokine release syndrome.

[0127] In various embodimentexamples, treatment with the IL-10 mutein reduces the suppression of TNF-alpha production in myeloid cells, reduces levels of CD8+ T cell stimulation, and/or reduces the level of B cell stimulation compared to wt IL-10. In various embodimentexamples, treatment with the IL-10 mutein antigen binding protein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, suppresses TNF- α production in myeloid cells. In various embodimentexamples, treatment with IL-10 mutein antigen binding protein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, suppresses TNF- α production in myeloid cells, while reducing CD8+ T cell and B cell activation. In various embodimentexamples, the treatment inhibits TNF- α production in myeloid cells, without CD8+ T cell stimulation and/or B cell stimulation in the subject. In various embodimentexamples, the treatment reduces the levels of TNF- α in the subject.

[0128] In various embodimentexamples, the treatment is administered intravenously or subcutaneously. In various embodimentexamples, the treatment is administered once weekly, once every two weeks, once every three weeks, once every 4 weeks, once monthly, once every 3 months, or once every six months.

[0129] In various embodimentexamples, the methods comprise administering one or two additional therapeutic agents. In various embodimentexamples, the additional therapeutic agents are selected from corticosteroids, NSAIDs, analgesics, immunosuppressive agents, anti-inflammatory agents, TNF α inhibitors, IL-12/IL-23 inhibitors, IL-17 and IFN- γ .

[0130] The disclosure also provides a composition comprising an IL-10 mutein as described herein for use in treating an inflammatory disease. In certain embodimentexamples, the disclosure

provides use of a composition comprising an IL-10 mutein as described herein in the preparation of a medicament for treating an inflammatory disease.

[0131] Further contemplated is a composition comprising an anti-TREM-1 antibody or antigen-binding fragment as described herein for use in treating an inflammatory disease. In certain embodimentexamples, the disclosure provides use of a composition comprising an anti-TREM-1 antibody or antigen-binding fragment thereof as described herein in the preparation of a medicament for treating an inflammatory disease.

[0132] Also contemplated is a composition comprising an anti-TREM-1 antibody or antigen-binding fragment of as described herein in combination with an anti-IL-10 mutein as described herein for use in treating an inflammatory disease. In various embodimentexamples, the disclosure provides use of composition comprising an anti-TREM-1 antibody or antigen-binding fragment as described herein in combination with an anti-IL-10 mutein as described herein in preparation of a medicament for treating an inflammatory disease.

[0133] Also contemplated is a composition comprising an antigen binding protein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, as described herein for use in treating an inflammatory disease. Further contemplated is use of a composition comprising an antigen binding protein as described herein, for example an anti-TREM-1/IL-10 mutein antigen binding protein, in the preparation of a medicament for treating an inflammatory disease.

[0134] In various embodimentexamples, the inflammatory disease is inflammatory bowel disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome, rheumatoid arthritis, psoriasis, psoriatic arthritis, or cytokine release syndrome (CRS). In one embodimentexample, the inflammatory disease is ulcerative colitis. In one embodimentexample, the inflammatory disease is Crohn's disease. In one embodimentexample, the inflammatory disease is irritable bowel syndrome. In one embodimentexample, the inflammatory disease is rheumatoid arthritis. In one embodimentexample, the inflammatory disease is psoriasis. In one embodimentexample, the inflammatory disease is psoriatic arthritis. In one embodimentexample, the inflammatory disease is cytokine release syndrome.

[0135] It is understood that each feature or embodimentexample, or combination, described herein is a non-limiting, illustrative example of any of the aspectexamples of the invention disclosure and, as such, is meant to be combinable with any other feature or embodimentexample, or combination, described herein. For example, where features are described with language such as “one embodimentexample”, “some exampleembodiments”, “certain exampleembodiments”, “further exampleembodiment”, “specific exemplary exampleembodiments”, and/or “another exampleembodiment”, each of these types of examples embodiments is a non-limiting example of a feature that is intended to be combined with any other feature, or

combination of features, described herein without having to list every possible combination. Such features or combinations of features apply to any of the ~~aspect~~examples of the ~~invention~~disclosure. Where examples of values falling within ranges are disclosed, any of these examples are contemplated as possible endpoints of a range, any and all numeric values between such endpoints are contemplated, and any and all combinations of upper and lower endpoints are envisioned.

[0136] The headings herein are for the convenience of the reader and not intended to be limiting. Additional ~~aspect~~examples, ~~embodiments~~, and variations of the ~~invention~~disclosure will be apparent from the Detailed Description and/or Drawing and/or claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0137] Figures 1A-1C show exemplary schematic drawings of bivalent and monovalent anti-TREM1 mAb/IL-10 mutein antigen binding proteins. Figure 1D illustrates the location of the IL-10 mutein attachment to the antigen binding protein.

[0138] Figure 2 shows that both bivalent and monovalent TREM-1 binding significantly enhanced IL-10 mutein suppression of monocyte activation.

[0139] Figures 3A-3B illustrate that anti-TREM-1 mAb/IL-10 mutein antigen binding proteins did not stimulate CD8+ T cell (Figure 3A) and B cell (Figure 3B) activation.

[0140] Figures 4A-4H illustrate that TREM-1 binding significantly enhanced IL-10 mutein suppression of monocyte activation for different fusion protein constructs.

[0141] Figures 5A-5B show IL-10 mutein potency on human (Fig. 5A) or mouse (Fig. 5B) monocytes, as demonstrated by TNF levels, is improved through TREM-1 binding of the fusion protein compared to antibody or IL-10 mutein alone.

[0142] Figures 6A-6D shows inhibition of ligand (PGLYRP1/PGN) mediated TREM-1 signaling by anti-human TREM-1 antibodies in human (Figure 6C-6D) or cyno (Figure 6A-6B) PBMCs as measured by TNF alpha release.

[0143] Figure 7 shows inhibition by anti-human TREM-1 Fabs of ligand (PGLYRP1/PGN) mediated signaling in a cell line overexpressing human TREM-1/DAP12 as measured by phosphorylation of spleen tyrosine kinase (pSYK).

DETAILED DESCRIPTION

N; GASTRAT (SEQ ID NO: 2219); DASNLET (SEQ ID NO: 2220); and AASRLQS (SEQ ID NO: 2221).

[0185] In various embodiments, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a light chain variable region comprising a LCDR3 amino acid sequence selected from the group consisting of QX₁X₂X₃X₄X₅X₆PX₇T (SEQ ID NO: 2201); wherein X₁ is Q, H or E, wherein X₂ is F or Y, wherein X₃ is K, Y or I, wherein X₄ is N, T, L, I, or M; wherein X₅ is W, F, H or Y, wherein X₆ is absent or P; wherein X₇ is W, N, Y, H or L;

QX₁YX₂X₃X₄PX₅T~~QX₁YX₂X₃X₄PX₅T~~ (SEQ ID NO: 2207), wherein X₁ is Q or H, wherein X₂ is D, A or G, wherein X₃ is N or K; wherein X₄ is L or I, and wherein X₅ is I or L; QQFKNWPPT (SEQ ID NO: 2222); QHYDNLPT (SEQ ID NO: 2223); LQAHGFPWT (SEQ ID NO: 2224); QQYDNLPLT (SEQ ID NO: 2225) and QFWPPWT (SEQ ID NO: 2226).

[0186] In various embodiments, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR1 amino acid sequence selected from the group consisting of X₁X₂X₃MX₄ (SEQ ID NO: 2202), wherein X₁ is A, R, T or S, wherein X₂ is Y or N, wherein X₃ is A or W, and wherein X₄ is S or N; a sequence X₁YDIN (SEQ ID NO: 2208), wherein X₁ is R or S; GYYX₁H (SEQ ID NO: 2723), wherein X₁ is M or I; AYAMS (SEQ ID NO: 2227); RYDIN (SEQ ID NO: 2228); and SYWMS (SEQ ID NO: 2229).

[0187] In various embodiments, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR2 amino acid sequence selected from the group consisting of X₁X₂X₃X₄X₅X₆ X₇ X₈ X₉YYX₁₀ X₁₁X₁₂VKG (SEQ ID NO: 2205), wherein X₁ is T, E, or S, wherein X₂ is absent or is M, V, or I, wherein X₃ is S, R or K, wherein X₄ is G or Q, wherein X₅ is S, D or H, wherein X₆ is G, S L, or A, wherein X₇ is S, G, or R, wherein X₈ is T, S, P or E, wherein X₉ is T or I, wherein X₁₀ is A or V, wherein X₁₁ is D or E, and wherein X₁₂ is S or A; X₁X₂NPX₃X₄GX₅X₆GX₇X₈ X₉X₁₀FX₁₁X₁₂ (SEQ ID NO: 2209), wherein X₁ is W or R, wherein X₂ is M or L, wherein X₃ is N, Q, or K, wherein X₄ is S, A, or R, wherein X₅ is N, or Q, wherein X₆ is S, A, or T, wherein X₇ is S, Q, or Y, wherein X₈ is V or T, wherein X₉ is Q or K, wherein X₁₀ is K or N, wherein X₁₁ is R or Q, and wherein X₁₂ is G or D; TSGSGSTTYADSVKG (SEQ ID NO: 2230); WMNPNSGNSSVQKFRG (SEQ ID NO: 2231); NIKQDGSEEYYVDSVKG (SEQ ID NO: 2232); and TSGSGTTYADSVKG (SEQ ID NO: 2669).

[0188] In various embodiments, the TREM-1 antibody comprises an antigen binding domain comprising a sequence having a heavy chain variable region comprising a HCDR3 amino acid sequence selected from the group consisting of X₁X₂X₃X₄X₅X₆ X₇ F X₈YYX₉ (SEQ ID NO: 2203), wherein X₁ is V, E, A or G, wherein X₂ is A, F, Y or G, wherein X₃ is G, S, Y or W,

Group II	RASQGIRK WLA (SEQ ID NO: 2216)	AASRLQS (SEQ ID NO: 2221)	LQAHGFP WT (SEQ ID NO: 2224); QFWPPWT (SEQ ID NO: 2226)	SYWMS (SEQ ID NO: 2229)	NIKQDGSE EYYVDSVK G (SEQ ID NO: 2232); TSGSGTYY ADSVKG (SEQ ID NO: 2669)	DYGDSFDY (SEQ ID NO: 2673)
Group III	QASX ₁ DIX ₂ X ₃ X ₄ LN (SEQ ID NO: 2204)	X ₁ X ₂ X ₃ X ₄ LE T (SEQ ID NO: 2206)	~~QX₁YX₂X₃X₄~~ ~~PX₅TQX₄YX₃~~ ~~3-4-5-6-7~~ ~~XXPX₆T~~ (SEQ ID NO: 2207)	X ₁ YDIN (SEQ ID NO: 2208)	X ₁ X ₂ NPX ₃ X ₄ GX ₅ X ₆ GX ₇ X ₈ X ₉ X ₁₀ FX ₁₁ X ₁ ₂ (SEQ ID NO: 2209)	X ₁ X ₂ X ₃ X ₄ X ₅ X ₆ X ₇ X ₈ X ₉ X ₁₀ X ₁₁ X ₁₂ FX ₁₃ X ₁₄ (SEQ ID NO: 2210)
	QASQDIRK HLN (SEQ ID NO: 2213);	DASNLET (SEQ ID NO: 2220);	QHYDNLPI T (SEQ ID NO: 2223); QQYDNLPL T (SEQ ID NO: 2225)	RYDIN (SEQ ID NO: 2228)	WMNPNSG NSSVQKFR G (SEQ ID NO: 2231)	GGYTSSW RWYFDL (SEQ ID NO: 2671); GGYTSSW SRWYFDL (SEQ ID NO: 2672)

Example 4-Generation of IL-10 Mutein Antigen binding Proteins

[0351] Generation and selection of bivalent and monovalent anti-TREM-1 mAb/IL-10 mutein therapeutic fusions, the PK/PD of the fusions, and effects on colitis model with murine bivalent and monovalent anti-TREM-1 mAb/IL-10 mutein are evaluated.

[0352] IL-10 wild type, IL-10M1 or IL-10 muteins were fused to the C terminus of the anti-TREM-1 antibody Fc domain. For almost all fusions, the ultimate K residue is removed from the Fc region of the antibody (referred to as “desK”). In one example, the linker between the anti-TREM-1 antibody and the IL-10 variant is a GGGGS (G4S) (SEQ ID NO: 2725) and the internal IL-10 linker is GGGSGG (SEQ ID NO: 2676) (G3SG2).

- ii. a heavy chain CDR2 comprising an amino acid sequence TSGSGSTYYADSVKG (SEQ ID NO: 2230); and
- iii. a heavy chain CDR3 comprising an amino acid sequence VAGSNFLFDY (SEQ ID NO: 2670).

[0561] Paragraph 155. An isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence QASX₁DIX₂X₃X₄LN (SEQ ID NO: 2204), wherein X₁ is R or Q, wherein X₂ is R, S, N or F, wherein X₃ is K or N, and wherein X₄ is H, Y or D;
 - ii. a light chain CDR2 comprising an amino acid sequence X₁X₂X₃X₄LET (SEQ ID NO: 2206), wherein X₁ is D, G or H, wherein X₂ is A, V or T, wherein X₃ is S, A or Y, and wherein X₄ is T or N;
 - iii. a light chain CDR3 comprising an amino acid sequence QX₁YX₂X₃X₄PX₅TQX₆YX₇X₈PX₉T (SEQ ID NO: 2207), wherein X₁ is Q or H, wherein X₂ is D, A or G, wherein X₃ is N or K; wherein X₄ is L or I, and wherein X₅ is I or L; and
- d. comprises a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence X₁YDIN (SEQ ID NO: 2208), wherein X₁ is R or S;
 - ii. a heavy chain CDR2 comprising an amino acid sequence X₁X₂NPX₃X₄GX₅X₆GX₇X₈X₉X₁₀FX₁₁X₁₂ (SEQ ID NO: 2209), wherein X₁ is W or R, wherein X₂ is M or L, wherein X₃ is N, Q, or K, wherein X₄ is S, A, or R, wherein X₅ is N, or Q, wherein X₆ is S, A, or T, wherein X₇ is S, Q, or Y,

What is Claimed is:

1. ~~A human interleukin-10 (IL-10) mutein comprising an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 2, wherein said IL-10 mutein has at least one mutation selected from a mutation in helical loop AB, helical loop CD, helical loop DE, helix A, helix B, helix C, helix D, helix E and/or helix F.~~
2. ~~The IL-10 mutein of claim 2, wherein the mutation is one or more of R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, I87A, H14Q, F15Y, M22V, K49T, K49S, F56Y, K57N, Y59T, L60Q, Q63E, Q63L, E67C, Q70E, Q70K, M77R, M77V, Q79R, Q79C, D84R, A89P, H90E, H90Q, S93E, S93Q, T100R, L103E, H109D, R110P, R110Q, L112V, E115K, N116D, A127M, K130Q, I136C, Y137C, M154V, M156C, K157N, or N160D of SEQ ID NO: 2, optionally comprising addition of 6 amino acids between helix D and helix E.~~
3. ~~The IL-10 mutein of claim 1 or 2 wherein the IL-10 mutein has the amino acid sequence set out in any one of SEQ ID NOS: 3-10 or SEQ ID NOS: 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170, 2172, 2174, 2176, 2178, 2180, 2182, 2360, 2362, 2364, 2366, 2368, 2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436, 2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2538, 2540 or 2777-2791.~~
4. ~~An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the IL-10 mutein of any one of claims 1 to 3.~~
5. ~~An isolated antigen binding protein, wherein the antigen binding protein:~~
 - a. ~~is an antibody or antibody fragment;~~
 - b. ~~binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;~~
 - c. ~~comprises a light chain variable domain comprising:~~

- i. ~~a light chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 30, 50, 70, 90, 110, 130, 150, 170, 190, 210, 230, 250, 270, 290 and 2190;~~
- ii. ~~a light chain CDR2 comprising an amino acid sequence selected from SEQ ID NOS: 31, 51, 71, 91, 111, 131, 151, 171, 191, 211, 231, 251, 271, 291 and 2191;~~
- iii. ~~a light chain CDR3 comprising an amino acid sequence selected from SEQ ID NOS: 32, 52, 72, 92, 112, 132, 152, 172, 192, 212, 232, 252, 272, 292 and 2192; and~~
- d. ~~comprises a heavy chain variable domain comprising:~~
 - i. ~~a heavy chain CDR1 comprising an amino acid sequence selected from SEQ ID NOS: 36, 56, 76, 96, 116, 136, 156, 176, 196, 216, 236, 256, 276, 296 and 2196;~~
 - ii. ~~a heavy chain CDR2 comprising an amino acid sequence selected from SEQ ID NOS: 37, 57, 77, 97, 117, 137, 157, 177, 197, 217, 237, 257, 277, 297 and 2197; and~~
 - iii. ~~a heavy chain CDR3 comprising an amino acid sequence selected from SEQ ID NOS: 38, 58, 78, 98, 118, 138, 158, 178, 198, 218, 238, 258, 278, 298 and 2198.~~

6. ~~The antigen-binding protein of claim 5 wherein the antigen-binding protein comprises a set of CDR amino acid sequences selected from:~~

- i) ~~SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);~~
- ii) ~~SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);~~
- iii) ~~SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);~~
- iv) ~~SEQ ID NO: 90 (LCDR1), SEQ ID NO: 91 (LCDR2), SEQ ID NO: 92 (LCDR3), SEQ ID NO: 96 (HCDR1), SEQ ID NO: 97 (HCDR2) and SEQ ID NO: 98 (HCDR3);~~

- v) ~~SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);~~
- vi) ~~SEQ ID NO: 130 (LCDR1), SEQ ID NO: 131 (LCDR2), SEQ ID NO: 132 (LCDR3), SEQ ID NO: 136 (HCDR1), SEQ ID NO: 137 (HCDR2) and SEQ ID NO: 138 (HCDR3);~~
- vii) ~~SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);~~
- viii) ~~SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3);~~
- ix) ~~SEQ ID NO: 190 (LCDR1), SEQ ID NO: 191 (LCDR2), SEQ ID NO: 192 (LCDR3), SEQ ID NO: 196 (HCDR1), SEQ ID NO: 197 (HCDR2) and SEQ ID NO: 198 (HCDR3);~~
- x) ~~SEQ ID NO: 210 (LCDR1), SEQ ID NO: 211 (LCDR2), SEQ ID NO: 212 (LCDR3), SEQ ID NO: 216 (HCDR1), SEQ ID NO: 217 (HCDR2) and SEQ ID NO: 218 (HCDR3);~~
- xi) ~~SEQ ID NO: 230 (LCDR1), SEQ ID NO: 231 (LCDR2), SEQ ID NO: 232 (LCDR3), SEQ ID NO: 236 (HCDR1), SEQ ID NO: 237 (HCDR2) and SEQ ID NO: 238 (HCDR3);~~
- xii) ~~SEQ ID NO: 250 (LCDR1), SEQ ID NO: 251 (LCDR2), SEQ ID NO: 252 (LCDR3), SEQ ID NO: 256 (HCDR1), SEQ ID NO: 257 (HCDR2) and SEQ ID NO: 258 (HCDR3);~~
- xiii) ~~SEQ ID NO: 270 (LCDR1), SEQ ID NO: 271 (LCDR2), SEQ ID NO: 272 (LCDR3), SEQ ID NO: 276 (HCDR1), SEQ ID NO: 277 (HCDR2) and SEQ ID NO: 278 (HCDR3);~~
- xiv) ~~SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3); or~~
- xv) ~~SEQ ID NO: 2190 (LCDR1), SEQ ID NO: 2191 (LCDR2), SEQ ID NO: 2192 (LCDR3), SEQ ID NO: 2196 (HCDR1), SEQ ID NO: 2197 (HCDR2) and SEQ ID NO: 2198 (HCDR3).~~

7. ~~The antigen-binding protein of claim 5 or 6 comprising:~~
- a. ~~a light chain variable domain comprising an amino acid sequence selected from the group consisting of:~~
 - i. ~~a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185;~~
 - ii. ~~a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185; or~~
 - iii. ~~a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279, 299 and 2183; and~~
 - b. ~~a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:~~
 - i. ~~a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186;~~
 - ii. ~~a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186; or~~
 - iii. ~~a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300 and 2184.~~
8. ~~The antigen binding protein of any one of claims 5 to 7 wherein the antigen binding protein comprises:~~
- i) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 41 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 42;~~

- ii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 61 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 62;~~
- iii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 81 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 82;~~
- iv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 101 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 102;~~
- v) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 121 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 122;~~
- vi) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 141 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 142;~~
- vii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 161 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 162;~~
- viii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 181 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 182;~~
- ix) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 201 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 202;~~
- x) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 221 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 222;~~
- xi) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 241 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 242;~~
- xii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 261 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 262;~~

- xiii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 281 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 282;~~
- xiv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 301 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 302; or~~
- xv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 2185 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 2186.~~

9. ~~An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain of any one of claims 5 to 8, the heavy chain of any one of claims 5 to 8, or both.~~

10. ~~An antigen binding protein comprising an antigen binding moiety and one or two IL-10 moieties wherein:~~

- a. ~~the antigen binding moiety is an antibody or antibody fragment,~~
- b. ~~each IL-10 moiety is independently monovalent or bivalent,~~
- c. ~~each IL-10 moiety is independently selected from one or more human IL-10 muteins having sequences that are 90% identical to SEQ ID NO: 2, and~~
- d. ~~at least one IL-10 moiety is covalently bound to the antigen binding moiety.~~

11. ~~An antigen binding protein comprising:~~

- ~~— (a) a polypeptide sequence having the formula A-L-M or M-L-A, wherein~~
 - i) ~~A is an immunoglobulin heavy chain of an IgG antibody that binds to a TREM-1 protein set out in SEQ ID NO: 20,~~
 - ii) ~~L is a linker peptide comprising from 4 to 20 amino acids and~~
 - iii) ~~M is a mutein of IL-10 having at least 90% sequence identity to wt IL-10 set out in SEQ ID NO: 2; and~~

- ~~— (b) an immunoglobulin light chain of an IgG antibody that binds TREM-1 protein set out in SEQ ID NO: 20,~~

~~wherein the immunoglobulin heavy chain of (a) and the immunoglobulin light chain of (b) form an IgG antibody moiety that binds TREM-1, wherein the protein comprises one or two~~

~~molecules of the polypeptide of (a) and one or two molecules of the light chain of (b), optionally wherein only 1 polypeptide of (a) comprises an M moiety.~~

~~12. The antigen binding protein of claim 10 or 11 wherein:~~

- ~~a. each IL-10 moiety comprises an amino acid sequence that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 2, and~~
- ~~b. each IL-10 moiety independently comprises at least one mutation selected from a mutation in helical loop AB, helical loop CD, helical loop DE, helix A, helix B, helix C, helix D, helix E and/or helix F.~~

~~13. The antigen binding protein of any one of claims 10 to 12, wherein each IL-10 moiety independently comprises:~~

- ~~i) a mutation in one or more of residues N10, H14, F15, P20, M22, L23, R24, R27, D28, K34, T35, Q38, M39, K40, D41, Q42, L43, D44, N45, L46, L47, L48, K49, F56, K57, Y59, L60, Q63, E67, Q70, M77, Q79, N82, Q83, D84, P85, D86, I87, A89, H90, S93, T100, L103, H109, R110, L112, E115, N116, A127, K130, I136, Y137, K138, S141, E142, D144, I145, E151, M154, M156, K157, or N160 of SEQ ID NO: 2 or an addition of 4-8 amino acids between helix D and helix E; and/or~~
- ~~ii) one or more mutations selected from the group consisting of N10Q, N10I, N10K, R27L, K34D, D41G, L46K, Q38E, Q38R, Q38D, K138L, K138D, I87A, H14Q, F15Y, M22V, K49T, K49S, F56Y, K57N, Y59T, L60Q, Q63E, Q63L, E67C, Q70E, Q70K, M77R, M77V, Q79R, Q79C, D84R, A89P, H90E, H90Q, S93E, S93Q, T100R, L103E, H109D, R110P, R110Q, L112V, E115K, N116D, N110Q, A127M, K130Q, I136C, Y137C, M154V, M156C, K157N, or N160D of SEQ ID NO: 2, optionally comprising an addition of six amino acids between helix D and helix E.~~

~~14. The antigen binding protein of any one of claims 10 to 13 wherein the IL-10 moiety has the amino acid sequence set out in any one of SEQ ID NOS: 3-10 or SEQ ID NOS: 2138, 2140, 2142, 2144, 2146, 2148, 2150, 2152, 2154, 2156, 2158, 2160, 2162, 2164, 2166, 2168, 2170, 2172, 2174, 2176, 2178, 2180, 2182, 2360, 2362, 2364, 2366, 2368, 2370, 2372, 2374, 2376, 2378, 2380, 2382, 2384, 2386, 2388, 2390, 2392, 2394, 2396, 2398, 2400, 2402, 2404, 2406, 2408, 2410, 2412, 2414, 2416, 2418, 2420, 2422, 2424, 2426, 2428, 2430, 2432, 2434, 2436,~~

~~2438, 2440, 2442, 2444, 2446, 2448, 2450, 2452, 2454, 2456, 2458, 2460, 2462, 2464, 2466, 2468, 2470, 2472, 2474, 2476, 2478, 2480, 2482, 2484, 2486, 2488, 2490, 2492, 2494, 2496, 2500, 2502, 2504, 2506, 2508, 2510, 2512, 2514, 2516, 2518, 2520, 2522, 2524, 2526, 2528, 2530, 2532, 2534, 2536, 2538, 2540 or 2777-2791.~~

~~15. The antigen binding protein of any one of claims 10 to 14 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085.~~

~~16. The antigen binding protein of any one of claims 10 to 15 that has a light chain amino acid sequence set out in any one of SEQ ID NOS: 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.~~

~~17. The antigen binding protein of any one of claims 10 to 16 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085 and a corresponding light chain amino acid sequence set out in SEQ ID NOS: 864, 866,~~

~~868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.~~

~~18. The antigen binding protein of any one of claims 10 to 14 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 1883, 1885, 1887, 1889, 1891, 1893, 1895, 1897, 1899, 1901, 1903, 1905, 1907, 1909, 1911, 1913, 1915, 1917, 1919, 1921, 1923, 1925, 1927, 1929, 1931, 1933, 1935, 1937, 1939, 1941, 1943, 1945, 1947, 1949, 1951, 1953, 1955, 1957, 1959, 1961, 1963, 1965, 1967, 1969, 1971, 1973, 1975, 1977, 1979, 1981, 1983, 1985, 1987, 1989, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, and 2007.~~

~~19. The antigen binding protein of any one of claims 10 to 14 or 18 that has the light chain amino acid sequence set out in any one of SEQ ID NOS: 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605.~~

~~20. The antigen binding protein of any one of claims 10 to 14 or 18 to 19 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 1883, 1885, 1887, 1889, 1891, 1893, 1895, 1897, 1899, 1901, 1903, 1905, 1907, 1909, 1911, 1913, 1915, 1917, 1919, 1921, 1923, 1925, 1927, 1929, 1931, 1933, 1935, 1937, 1939, 1941, 1943, 1945, 1947, 1949, 1951, 1953, 1955, 1957, 1959, 1961, 1963, 1965, 1967, 1969, 1971, 1973, 1975, 1977, 1979, 1981, 1983, 1985, 1987, 1989, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, and 2007, and a corresponding light chain amino acid sequence set out in SEQ ID NOS: 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605.~~

~~21. The antigen binding protein of any one of claims 10 to 14 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2011, 2013, 2015, 2017, 2019, 2021, 2026, 2025, 2027, 2029, 2031, 2033, 2035, 2037, 2039, 2041, 2043, 2045, 2047, 2049, 2051, 2053, 2055, 2057, 2059, 2061, 2063, 2065, 2067, 2069, 2071, 2073, 2075, 2077, 2079, 2081, 2083, 2085, 2087, 2089, 2091, 2093, 2095, 2097, 2099, 2101, 2103, 2105, 2107, 2109, 2111, 2113, 2115, 2117, 2119, 2121, 2123, 2125, 2127, 2129, 2131, 2133, and 2135.~~

~~22. The antigen binding protein of any one of claims 10 to 14 or 21 that has a light chain amino acid sequence set out in any one of SEQ ID NOS: 2233, 2235, 2237, 2239, 2241, 2243, 2245, 2247, 2249, 2251, 2253, 2255, 2257, 2259, 2261, 2263, 2265, 2267, 2269, 2271, 2273, 2275, 2277, 2279, 2281, 2283, 2285, 2287, 2289, 2291, 2293, 2295, 2297, 2299, 2301, 2303, 2305, 2307, 2309, 2311, 2313, 2315, 2317, 2319, 2321, 2323, 2325, 2327, 2329, 2331, 2333, 2335, 2337, 2339, 2341, 2343, 2345, 2347, 2349, 2351, 2353, 2355, and 2357.~~

~~23. The antigen binding protein of any one of claims 10 to 14 or 21 to 22 that has a heavy chain amino acid sequence set out in any one of SEQ ID NOS: 2011, 2013, 2015, 2017, 2019, 2021, 2026, 2025, 2027, 2029, 2031, 2033, 2035, 2037, 2039, 2041, 2043, 2045, 2047, 2049, 2051, 2053, 2055, 2057, 2059, 2061, 2063, 2065, 2067, 2069, 2071, 2073, 2075, 2077, 2079, 2081, 2083, 2085, 2087, 2089, 2091, 2093, 2095, 2097, 2099, 2101, 2103, 2105, 2107, 2109, 2111, 2113, 2115, 2117, 2119, 2121, 2123, 2125, 2127, 2129, 2131, 2133, and 2135, and a corresponding light chain amino acid sequence set out in SEQ ID NOS: 2233, 2235, 2237, 2239, 2241, 2243, 2245, 2247, 2249, 2251, 2253, 2255, 2257, 2259, 2261, 2263, 2265, 2267, 2269, 2271, 2273, 2275, 2277, 2279, 2281, 2283, 2285, 2287, 2289, 2291, 2293, 2295, 2297, 2299, 2301, 2303, 2305, 2307, 2309, 2311, 2313, 2315, 2317, 2319, 2321, 2323, 2325, 2327, 2329, 2331, 2333, 2335, 2337, 2339, 2341, 2343, 2345, 2347, 2349, 2351, 2353, 2355, and 2357.~~

~~24. The antigen binding protein of any one of claims 10 to 23 wherein the antigen binding moiety is an anti-TREM-1 antigen-binding moiety comprising:~~

~~a. a light chain variable domain comprising:~~

- i. ~~a light chain CDR1 sequence comprising an amino acid sequence selected from SEQ ID NOS: 30, 50, 70, 90, 110, 130, 150, 170, 190, 210, 230, 250, 270, 290 and 2190;~~
- ii. ~~a light chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NOS: 31, 51, 71, 91, 111, 131, 151, 171, 191, 211, 231, 251, 271, 291 and 2190;~~
- iii. ~~a light chain CDR3 sequence comprising an amino acid sequence selected from SEQ ID NOS: 32, 52, 72, 92, 112, 132, 152, 172, 192, 212, 232, 252, 272, 292 and 2192; and~~
- b. ~~a heavy chain variable domain comprising:~~
 - i. ~~a heavy chain CDR1 sequence comprising an amino acid sequence selected from SEQ ID NOS: 36, 56, 76, 96, 116, 136, 156, 176, 196, 216, 236, 256, 276, 296 and 2196;~~
 - ii. ~~a heavy chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NOS: 37, 57, 77, 97, 117, 137, 157, 177, 197, 217, 237, 257, 277, 297 and 2197; and~~
 - iii. ~~a heavy chain CDR3 sequence comprising an amino acid sequence selected from SEQ ID NOS: 38, 58, 78, 98, 118, 138, 158, 178, 198, 218, 238, 258, 278, 298 and 2198.~~

25. ~~The antigen-binding protein of any one of claims 10 to 24 wherein the antigen-binding moiety is an anti-TREM-1 antigen-binding moiety comprising a set of CDR amino acid sequences selected from:~~

- i) ~~SEQ ID NO: 30 (LCDR1), SEQ ID NO: 31 (LCDR2), SEQ ID NO: 32 (LCDR3), SEQ ID NO: 36 (HCDR1), SEQ ID NO: 37 (HCDR2) and SEQ ID NO: 38 (HCDR3);~~

- ~~ii) SEQ ID NO: 50 (LCDR1), SEQ ID NO: 51 (LCDR2), SEQ ID NO: 52 (LCDR3), SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2) and SEQ ID NO: 58 (HCDR3);~~
- ~~iii) SEQ ID NO: 70 (LCDR1), SEQ ID NO: 71 (LCDR2), SEQ ID NO: 72 (LCDR3), SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2) and SEQ ID NO: 78 (HCDR3);~~
- ~~iv) SEQ ID NO: 90 (LCDR1), SEQ ID NO: 91 (LCDR2), SEQ ID NO: 92 (LCDR3), SEQ ID NO: 96 (HCDR1), SEQ ID NO: 97 (HCDR2) and SEQ ID NO: 98 (HCDR3);~~
- ~~v) SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), SEQ ID NO: 112 (LCDR3), SEQ ID NO: 116 (HCDR1), SEQ ID NO: 117 (HCDR2) and SEQ ID NO: 118 (HCDR3);~~
- ~~vi) SEQ ID NO: 130 (LCDR1), SEQ ID NO: 131 (LCDR2), SEQ ID NO: 132 (LCDR3), SEQ ID NO: 136 (HCDR1), SEQ ID NO: 137 (HCDR2) and SEQ ID NO: 138 (HCDR3);~~
- ~~vii) SEQ ID NO: 150 (LCDR1), SEQ ID NO: 151 (LCDR2), SEQ ID NO: 152 (LCDR3), SEQ ID NO: 156 (HCDR1), SEQ ID NO: 157 (HCDR2) and SEQ ID NO: 158 (HCDR3);~~
- ~~viii) SEQ ID NO: 170 (LCDR1), SEQ ID NO: 171 (LCDR2), SEQ ID NO: 172 (LCDR3), SEQ ID NO: 176 (HCDR1), SEQ ID NO: 177 (HCDR2) and SEQ ID NO: 178 (HCDR3);~~
- ~~ix) SEQ ID NO: 190 (LCDR1), SEQ ID NO: 191 (LCDR2), SEQ ID NO: 192 (LCDR3), SEQ ID NO: 196 (HCDR1), SEQ ID NO: 197 (HCDR2) and SEQ ID NO: 198 (HCDR3);~~

- ~~x) SEQ ID NO: 210 (LCDR1), SEQ ID NO: 211 (LCDR2), SEQ ID NO: 212 (LCDR3), SEQ ID NO: 216 (HCDR1), SEQ ID NO: 217 (HCDR2) and SEQ ID NO: 218 (HCDR3);~~
- ~~xi) SEQ ID NO: 230 (LCDR1), SEQ ID NO: 231 (LCDR2), SEQ ID NO: 232 (LCDR3), SEQ ID NO: 236 (HCDR1), SEQ ID NO: 237 (HCDR2) and SEQ ID NO: 238 (HCDR3);~~
- ~~xii) SEQ ID NO: 250 (LCDR1), SEQ ID NO: 251 (LCDR2), SEQ ID NO: 252 (LCDR3), SEQ ID NO: 256 (HCDR1), SEQ ID NO: 257 (HCDR2) and SEQ ID NO: 258 (HCDR3);~~
- ~~xiii) SEQ ID NO: 270 (LCDR1), SEQ ID NO: 271 (LCDR2), SEQ ID NO: 272 (LCDR3), SEQ ID NO: 276 (HCDR1), SEQ ID NO: 277 (HCDR2) and SEQ ID NO: 278 (HCDR3);~~
- ~~xiv) SEQ ID NO: 290 (LCDR1), SEQ ID NO: 291 (LCDR2), SEQ ID NO: 292 (LCDR3), SEQ ID NO: 296 (HCDR1), SEQ ID NO: 297 (HCDR2) and SEQ ID NO: 298 (HCDR3); or~~
- ~~xv) SEQ ID NO: 2190 (LCDR1), SEQ ID NO: 2191 (LCDR2), SEQ ID NO: 2192 (LCDR3), SEQ ID NO: 2196 (HCDR1), SEQ ID NO: 2197 (HCDR2) and SEQ ID NO: 2198 (HCDR3).~~

~~26. The antigen binding protein of any one of claims 10 to 25 wherein the anti-TREM-1 antigen-binding moiety comprises:~~

- ~~a. a light chain variable domain comprising an amino acid sequence selected from the group consisting of:~~
 - ~~i. a sequence at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185;~~

- ii. ~~a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 41, 61, 81, 101, 121, 141, 161, 181, 201, 221, 241, 261, 281, 301 and 2185;~~
 - iii. ~~a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic acid sequence selected from SEQ ID NOS: 39, 59, 79, 99, 119, 139, 159, 179, 199, 219, 239, 259, 279, 299 and 2183; and~~
 - b. ~~a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of:~~
 - i. ~~a sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186;~~
 - ii. ~~a sequence encoded by a polynucleotide sequence that is at least 80% identical to an amino acid sequence selected from SEQ ID NOS: 42, 62, 82, 102, 122, 142, 162, 182, 202, 222, 242, 262, 282, 302 and 2186;~~
 - iii. ~~a sequence encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of a nucleic sequence selected from SEQ ID NOS: 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300 and 2184.~~
27. ~~The antigen binding protein of any one of claims 10 to 26 wherein the antigen binding moiety is an anti-TREM-1 antigen-binding moiety comprising:~~
- i) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 41 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 42;~~
 - ii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 61 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 62;~~

- iii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 81 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 82;~~
- iv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 101 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 102;~~
- v) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 121 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 122;~~
- vi) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 141 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 142;~~
- vii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 161 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 162;~~
- viii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 181 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 182;~~
- ix) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 201 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 202;~~
- x) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 221 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 222;~~
- xi) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 241 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 242;~~
- xii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 261 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 262;~~
- xiii) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 281 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 282;~~

- xiv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 301 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 302; or~~
 - xv) ~~an amino acid sequence at least 90% identical to a light chain variable domain set out in SEQ ID NO: 2185 and an amino acid sequence at least 90% identical to a heavy chain variable domain set out in SEQ ID NO: 2186~~
28. ~~The antigen binding protein of claim any one of claims 24 to 27, wherein:~~
- a. ~~the antigen binding protein comprises two light chains and two heavy chains:~~
 - b. ~~each heavy chain comprises an IL-10 moiety attached at the C-terminus of the heavy chain;~~
 - c. ~~each heavy chain-IL-10 moiety antigen binding protein comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS: 863, 865, 867, 869, 871, 873, 875, 877, 879, 881, 883, 885, 887, 889, 891, 893, 895, 897, 899, 901, 903, 905, 907, 909, 911, 913, 915, 917, 919, 921, 923, 925, 927, 929, 931, 933, 935, 937, 939, 941, 943, 945, 947, 949, 951, 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1017, 1019, 1021, 1023, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, 1051, 1053, 1055, 1057, 1059, 1061, 1063, 1065, 1067, 1069, 1071, 1073, 1075, 1077, 1079, 1081, 1083, and 1085; and~~
 - d. ~~each light chain-IL-10 moiety comprises an amino acid sequence at least 90% identical to a sequence selected from SEQ ID NOS: 864, 866, 868, 870, 872, 874, 876, 878, 880, 882, 884, 886, 888, 890, 892, 894, 896, 898, 900, 902, 904, 906, 908, 910, 912, 914, 916, 918, 920, 922, 924, 926, 928, 930, 932, 934, 936, 938, 940, 942, 944, 946, 948, 950, 952, 954, 956, 958, 960, 962, 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1018, 1020, 1022, 1024, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, 1052, 1054, 1056, 1058, 1060, 1062, 1064, 1066, 1068, 1070, 1072, 1074, 1076, 1078, 1080, 1082, 1084, and 1086.~~
29. ~~The antigen binding protein of any one of claims 10 to 14 or 24 to 27, wherein the antigen binding protein has a heavy chain-IL-10 moiety amino acid sequence selected from the~~

~~group consisting of SEQ ID NOS: 2137, 2139, 2141, 2143, 2145, 2147, 2149, 2151, 2153, 2155, 2157, 2159, 2161, 2163, 2165, 2167, 2169, 2171, 2173, 2175, 2177, 2179, 2181, 2359, 2361, 2363, 2365, 2367, 2369, 2371, 2373, 2375, 2377, 2379, 2381, 2383, 2385, 2387, 2389, 2391, 2393, 2395, 2397, 2399, 2401, 2403, 2405, 2407, 2409, 2411, 2143, 2415, 2417, 2419, 2421, 2423, 2425, 2427, 2429, 2431, 2433, 2435, 2437, 2439, 2441, 2443, 2445, 2447, 2449, 2451, 2453, 2455, 2457, 2459, 2461, 2463, 2465, 2467, 2469, 2471, 2473, 2475, 2477, 2479, 2481, 2483, 2485, 2487, 2489, 2491, 2493, 2495, 2497, 2498, 2499, 2501, 2503, 2505, 2507, 2509, 2511, 2513, 2515, 2517, 2519, 2521, 2523, 2525, 2527, 2529, 2531, 2533, 2535, 2537, 2539 and 2726-2776.~~

~~30. The antigen binding protein of any one of claims 10 to 14 or 24 to 28, wherein the antigen binding protein has a heavy chain-IL-10 moiety amino acid sequence selected from the group consisting of SEQ ID NOS: 2727-2732.~~

~~31. The antigen binding protein of claim 30 comprising the heavy chain amino acid sequence of SEQ ID NO: 2727 or 2728, and the light chain amino acid sequence set out in SEQ ID NO: 976 or SEQ ID NO: 2554.~~

~~32. The antigen binding protein of claim 30 comprising the heavy chain amino acid sequence of SEQ ID NO: 2729, 2730, 2731 or 2732, and the light chain amino acid sequence set out in and SEQ ID NO: 992 or SEQ ID NO: 2555.~~

~~33. An antigen binding protein comprising an antigen-binding moiety and one or two IL-10 moieties wherein:~~

- ~~a. the antigen-binding moiety is an antibody or antibody fragment;~~
- ~~b. each IL-10 moiety is independently monovalent or bivalent;~~
- ~~c. each IL-10 moiety is independently selected from one or more human IL-10 muteins having sequences that are 90% identical to SEQ ID NO: 2;~~
- ~~d. at least one IL-10 moiety is covalently bound to the antigen-binding moiety, and/or~~
- ~~e. the antigen-binding moiety competes for binding to a human TREM-1 protein with the antigen-binding moiety of any one of claims 24 to 27.~~

~~34. — An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain region of the antigen binding protein of any one of claims 10-33, the light chain region of the antigen binding protein of any one of claims 10-33, or both.~~

~~35. — A method of treating an inflammatory disease in a subject in a need thereof comprising administering~~

- ~~i) an IL-10 mutein of any one of claims 1-3;~~
- ~~ii) an anti-TREM-1 antigen binding protein of any of claims 5-8; or~~
- ~~iii) an antigen binding protein of any one of claims 10-33.~~

~~36. — The method of claim 35, wherein the inflammatory disease is selected from the group consisting of inflammatory bowel disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome, rheumatoid arthritis, psoriasis, psoriatic arthritis, and cytokine release syndrome (CRS).~~

~~37. — A composition for use in treating an inflammatory disease comprising~~

- ~~i) an IL-10 mutein of any one of claims 1-3;~~
- ~~ii) an anti-TREM-1 antigen binding protein of any of claims 5-8; or~~
- ~~iii) an antigen binding protein of any one of claims 10-33.~~

~~38. — Use of a composition comprising an IL-10 mutein of any one of claims 1-3 in the preparation of a medicament for treating an inflammatory disease.~~

~~39. — Use of a composition in the preparation of a medicament for treating an inflammatory disease, the composition comprising:~~

- ~~i) an IL-10 mutein of any one of claims 1-3;~~
- ~~ii) an anti-TREM-1 antigen binding protein of any of claims 5-8; or~~
- ~~iii) an antigen binding protein of any one of claims 10-33.~~

~~40. — Use of composition comprising an anti-TREM-1 antibody or antigen binding fragment of any one of claims 5-8 and 10-33 in combination with an anti-IL-10 mutein of any one of claims 1-3 in preparation of a medicament for treating an inflammatory disease.~~

41. An isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence $X_1ASQSX_2X_3X_4NLA$ (SEQ ID NO: 2199), wherein X_1 is R or Q, wherein X_2 is V or I, wherein X_3 is N or S, and wherein X_4 is S, H, I, V or A;
 - ii. a light chain CDR2 comprising an amino acid sequence GAX_1X_2RAT (SEQ ID NO: 2200), wherein X_1 is S or Y, and wherein X_2 is T or I; and
 - iii. a light chain CDR3 comprising an amino acid sequence $QX_1X_2X_3X_4X_5X_6PX_7T$ (SEQ ID NO: 2201); wherein X_1 is Q, H or E, wherein X_2 is F or Y, wherein X_3 is K, Y or I, wherein X_4 is N, T, L, I, or M; wherein X_5 is W, F, H or Y, wherein X_6 is absent or P; wherein X_7 is W, N, Y, H or L; and
- d. comprises a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence $X_1X_2X_3MX_4$ (SEQ ID NO: 2202), wherein X_1 is A, R, T or S, wherein X_2 is Y or N, wherein X_3 is A or W, and wherein X_4 is S or N;
 - ii. a heavy chain CDR2 comprising an amino acid sequence $X_1X_2X_3X_4X_5X_6X_7X_8X_9YYX_{10}X_{11}X_{12}VKG$ (SEQ ID NO: 2205), wherein X_1 is T, E, or S, wherein X_2 is absent or is M, V, or I, wherein X_3 is S, R or K, wherein X_4 is G or Q, wherein X_5 is S, D or H, wherein X_6 is G, S L, or A, wherein X_7 is S, G, or R, wherein X_8 is T, S, P or E, wherein X_9 is T or I, wherein X_{10} is A or V, wherein X_{11} is D or E, and wherein X_{12} is S or A; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence $X_1X_2X_3X_4X_5X_6X_7FX_8YYX_9$ (SEQ ID NO: 2203), wherein X_1 is V, E, A or G, wherein X_2 is A, F, Y or G, wherein X_3 is G, S, Y or W, wherein X_4 is S or R, wherein X_5 is

absent or is N, wherein X₆ is F, S, Y, or absent, wherein X₇ is L or F or absent, wherein X₈ is D or E, and wherein X₉ is Y, H or S.

42. The isolated antigen binding protein of claim 41, wherein the antigen binding protein comprises:

- a. a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence RASQSVNSNLA (SEQ ID NO: 2212);
 - ii. a light chain CDR2 comprising an amino acid sequence GASTRAT (SEQ ID NO: 2219);
 - iii. a light chain CDR3 comprising an amino acid sequence QQFKNWPPT (SEQ ID NO: 2222); and
- b. a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence AYAMS (SEQ ID NO: 2227);
 - ii. a heavy chain CDR2 comprising an amino acid sequence TSGSGSTTYADSVKG (SEQ ID NO: 2230); and
 - iii. a heavy chain CDR3 comprising an amino acid sequence VAGSNFLFDY (SEQ ID NO: 2670).

43. An isolated antigen binding protein, wherein the antigen binding protein:

- a. is an antibody or antibody fragment;
- b. binds to human TREM-1 having the amino acid sequence set forth in SEQ ID NO: 20;
- c. comprises a light chain variable domain comprising:

- i. a light chain CDR1 comprising an amino acid sequence QASX₁DIX₂X₃X₄LN (SEQ ID NO: 2204), wherein X₁ is R or Q, wherein X₂ is R, S, N or F, wherein X₃ is K or N, and wherein X₄ is H, Y or D;
 - ii. a light chain CDR2 comprising an amino acid sequence X₁X₂X₃X₄LET (SEQ ID NO: 2206), wherein X₁ is D, G or H, wherein X₂ is A, V or T, wherein X₃ is S, A or Y, and wherein X₄ is T or N;
 - iii. a light chain CDR3 comprising an amino acid sequence ~~QX₁YX₂X₃X₄YX₅YX₆T~~
QX₁YX₂X₃X₄PX₅T (SEQ ID NO: 2207), wherein X₁ is Q or H, wherein X₂ is D, A or G, wherein X₃ is N or K; wherein X₄ is L or I, and wherein X₅ is I or L;
and
- d. comprises a heavy chain variable domain comprising:
- i. a heavy chain CDR1 comprising an amino acid sequence X₁YDIN (SEQ ID NO: 2208), wherein X₁ is R or S;
 - ii. a heavy chain CDR2 comprising an amino acid sequence X₁X₂NPX₃X₄GX₅X₆GX₇X₈X₉X₁₀FX₁₁X₁₂ (SEQ ID NO: 2209), wherein X₁ is W or R, wherein X₂ is M or L, wherein X₃ is N, Q, or K, wherein X₄ is S, A, or R, wherein X₅ is N, or Q, wherein X₆ is S, A, or T, wherein X₇ is S, Q, or Y, wherein X₈ is V or T, wherein X₉ is Q or K, wherein X₁₀ is K or N, wherein X₁₁ is R or Q, and wherein X₁₂ is G or D; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence X₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂FX₁₃X₁₄ (SEQ ID NO: 2210); wherein X₁ is G, L or R, wherein X₂ is G, I, or R, wherein X₃ is Y, R, I, G, or A, wherein X₄ is T, S, Y, or V, wherein X₅ is S or Y, wherein X₆ is S, A, I, or R, wherein X₇ is W, A, or S, wherein X₈ is absent or is S, wherein X₉ is absent or is F, W, or Y, and wherein X₁₀ is R, S, H, K, or E, wherein X₁₁ is W, H, Y, or F, wherein X₁₂ is Y, V, A, or S, wherein X₁₃ is D or Q, and wherein X₁₄ is L, Y, I, or H.

44. The antigen binding protein of claim 43, wherein the antigen binding protein comprises:

- a. a light chain variable domain comprising:
 - i. a light chain CDR1 comprising an amino acid sequence QASQDIRKHLN (SEQ ID NO: 2213);
 - ii. a light chain CDR2 comprising an amino acid sequence DASNLET (SEQ ID NO: 2220); and
 - iii. a light chain CDR3 comprising an amino acid sequence QHYDNLPIIT (SEQ ID NO: 2223); and
- b. a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence RYDIN (SEQ ID NO: 2228);
 - ii. a heavy chain CDR2 comprising an amino acid sequence WMNPNSGNSSVQKFRG (SEQ ID NO: 2231); and
 - iii. a heavy chain CDR3 comprising an amino acid sequence GGYTSSWRWYFDL (SEQ ID NO: 2671) or GGYTSSWSRWYFDL (SEQ ID NO: 2672).