antigen-binding fragment, and a pharmaceutically acceptable carrier. Further examples provide for a method of treating inflammatory bowel disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or an antigen-binding fragment. In some examples, the inflammatory bowel disease comprises Crohn's Disease, ulcerative colitis, medically refractive-ulcerative colitis, or a combination thereof. In some examples, prior to administering the antibody or antigen-binding fragment to the subject, the subject over-expresses TL1A. In some examples, the subject comprises a risk variant associated with the inflammatory bowel disease.

[0005] In another example, provided herein is a polypeptide comprising: one or more complementarity determining regions selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 30, SEQ ID NO: 31, and SEQ ID NO: 32.

[0005a] In one aspect, provided herein is a humanized antibody or humanized antigen-binding fragment that binds human tumor necrosis factor-like protein 1A (TL1A), wherein the humanized antibody or humanized antigen-binding fragment comprises:~~competes~~ (a) a heavy chain variable region ~~for binding to the human TL1A with a reference antibody~~ comprising a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), and a heavy chain complementarity determining region 3 (HCDR3), wherein (i) the HCDR1 comprises a first amino acid sequence of **DTYMH**~~S~~ of SEQ ID NO~~S~~: 6; (ii) the HCDR2 comprises a second amino acid sequence of **PASGH** of SEQ ID NO. 7; and (iii) the HCDR3 comprises a third amino acid sequence of **SGGLPD** of SEQ ID NO. 8;~~ 8~~ and (b) a light chain variable region comprising a light chain complementarity determining region~~s~~ 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and a light chain complementarity determining region 3 (LCDR3), wherein (i) the LCDR1 comprises a fourth amino acid sequence of **ASSSVSYMY** of SEQ ID NO~~S~~: 14~~ 16~~; (ii) the LCDR2 comprises a fifth amino acid sequence of **ATSNLAS** of SEQ ID NO. 15; and (iii) the LCDR3 comprises a sixth amino acid sequence of **GNPRT** of SEQ ID NO. 16~~, wherein the humanized antibody or humanized antigen-binding fragment binds to human TL1A with a binding affinity (KD) of 1E-10 M or less~~.

[0006] In another example, provided herein is an antibody or antigen binding fragment that binds to the same region of human TL1A as a reference antibody comprising the heavy chain complementarity determining regions (CDRs) of SEQ ID NOs: 6 - 8 and the light chain complementarity determining regions (CDRs) of SEQ ID NOs: 14 - 16. In some examples, the reference antibody comprises a heavy chain variable domain of SEQ ID NO: 5 and a light chain variable domain of SEQ ID NO: 13. In some examples, the antibody or antigen-binding fragment is: a monoclonal antibody, a chimeric antibody, a CDR- grafted antibody, a humanized antibody, a Fab, a Fab', a F(ab')2, a Fv, a disulfide linked Fv, a scFv, a single domain antibody, a diabody, a multispecific antibody, a dual specific antibody, an anti-idiotypic antibody, a bispecific antibody, or a combination thereof. Further examples provide for a pharmaceutical composition comprising a therapeutically effective amount of the antibody or antigen-binding fragment, and a pharmaceutically acceptable carrier. Further examples provide for a method of treating inflammatory bowel

disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody or an antigen-binding fragment. In some examples, the inflammatory bowel disease comprises Crohn's Disease, ulcerative colitis, medically refractive-ulcerative colitis, or a combination thereof. In some examples, prior to administering the antibody or antigen-binding fragment to the subject, the subject over-expresses TL1A. In some examples, the subject comprises a risk variant associated with the inflammatory bowel disease.

[0007] In another example, provided herein is an antibody or antigen binding fragment that binds to the same region of human TL1A as a reference antibody comprising the heavy chain complementarity determining regions (CDRs) of SEQ ID NOs: 22 - 24 and the light chain

F(ab')2, a Fv, a disulfide linked Fv, a scFv, a single domain antibody, a diabody, a multispecific antibody, a dual specific antibody, an anti-idiotypic antibody, a bispecific antibody, or a combination thereof. In some examples, the inflammatory bowel disease comprises Crohn's Disease, ulcerative colitis, medically refractive-ulcerative colitis, or a combination thereof.

[0013b] In another aspect, provided herein is the antibody or an antigen-binding fragment as described herein for use in therapy.

[0013c] In another aspect, provided herein is the use of the antibody or an antigen-binding fragment as described herein in the manufacture of a medicament for treating an inflammatory bowel disease in a subject in need thereof.

[0013d] In another aspect, provided herein is a nucleic acid encoding the humanized antibody or humanized antigen-binding fragment as described herein.

BRIEF DESCRIPTION OF THE FIGURES

[0014] Exemplary embodiments are illustrated in referenced figures. It is intended that the embodiments and figures disclosed herein are to be considered illustrative rather than restrictive.

[0015] FIG. 1 depicts agarose gel electrophoresis of total RNA from the hybridoma 684842-3 (5C3D11). DNA marker, Marker III, is shown in Lane M and Total RNA of 684842-3 is shown in Lane R.

[0016] FIG. 2 depicts agarose gel electrophoresis of PCR products of 684842-3. DNA marker, Marker III, is shown in Lane M, the variable heavy chain (VH) of 684842-3 is shown in Lane 1, and the variable light chain (VL) of 684842-3 is shown in Lane 2.

[0017] FIG. 3 depicts an agarose gel electrophoresis of total RNA from hybridoma 684842-6 (9E12E5). DNA marker, Marker III, is shown in Lame M and Total RNA of 684842-6 is shown in Lane R.

[0018] FIG. 4 depicts an agarose gel electrophoresis of PCR products of 684842-6. DNA marker, Marker III, is shown in Lane M, the VH of 684842-6 is shown in Lane 1, and the VL of 684842-6 is shown in Lane 2.

[0019] FIG. 5 demonstrates the inhibition of human TL1A induced IFN-γ production by 9E12E5 (panel A) and 5C3D11 (panel B).

[0020] FIG. 6 demonstrates the recognition capability of 5C3D11 (panel A) and 9E12E5 (panel B), to murine TL1A.

CLAIMS

WHAT IS CLAIMED IS:

1. A humanized antibody or humanized antigen-binding fragment that binds human tumor necrosis factor-like protein 1A (TL1A), wherein the humanized antibody or humanized antigen-binding fragment comprises:~~competes for binding to the human TL1A with a reference antibody~~

(a) a heavy chain variable region comprising a heavy chain complementarity determining ~~regions~~ region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), and a heavy chain complementarity determining region 3 (HCDR3), wherein

(i) the HCDR1 comprises a first amino acid sequence of **DTYMH** of SEQ ID NO~~S~~: 6~~-8~~;

(ii) the HCDR2 comprises a second amino acid sequence of **PASGH** of SEQ ID NO. 7; and

(iii) the HCDR3 comprises a third amino acid sequence of **SGGLPD** of SEQ ID NO. 8; and

(b) a light chain variable region comprising a light chain complementarity determining region~~s~~ 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and a light chain complementarity determining region 3 (LCDR3), wherein

(i) the LCDR1 comprises a fourth amino acid sequence of **ASSSVSYMY** of SEQ ID NO~~S~~: 14~~-16~~;

(ii) the LCDR2 comprises a fifth amino acid sequence of **ATSNLAS** of SEQ ID NO. 15; and

(iii) the LCDR3 comprises a sixth amino acid sequence of **GNPRT** of SEQ ID NO. 16~~, wherein the humanized antibody or humanized antigen-binding fragment binds to human TL1A with a binding affinity (KD) of 1E-10 M or less~~.

2. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized antibody or humanized antigen-binding fragment is: a monoclonal antibody, ~~a chimeric antibody,~~ a CDR- grafted antibody, a Fab, a Fab', a F(ab')2, a Fv, a disulfide linked Fv, a scFv, ~~a single domain antibody,~~ a diabody, a multispecific antibody, a dual specific antibody, ~~an anti-idiotypic antibody,~~ a bispecific antibody, or a combination thereof.

3. The humanized antibody or humanized antigen-binding fragment of claim 1 or 2, wherein the ~~reference~~ humanized antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 5, and a light chain variable region comprising SEQ ID NO: 13.

4. The humanized antibody or humanized antigen-binding fragment of claim 1 or 2, wherein the humanized ~~reference~~ antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 35, and a light chain variable region comprising SEQ ID NO: 40.

5. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized ~~reference~~ antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 36, and a light chain variable region comprising SEQ ID NO: 41.

6. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized ~~reference~~ antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 37, and a light chain variable region comprising SEQ ID NO: 42.

7. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized ~~reference~~ antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 38, and a light chain variable region comprising SEQ ID NO: 43

8. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized ~~reference~~ antibody or humanized antigen-binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 39, and a light chain variable region comprising SEQ ID NO: 44.

9. The antibody or antigen-binding fragment of any one of claims 1-~~9~~8, for use in therapy.

10. Use of the antibody or antigen-binding fragment of any one of claims 1-9, in the ~~manfucature~~ manufacture of a medicament for treating an inflammatory bowel disease in a subject in need thereof.

11. The use of claim 10, wherein the inflammatory bowel disease comprises Crohn's Disease, ulcerative colitis, medically refractory-ulcerative colitis, or a combination thereof.

12. The use of claim 10 or 11, wherein the subject has previously undergone treatment with a second therapeutic agent.

13. The use of claim 12, wherein the second therapeutic agent comprises an anti-tumor necrosis factor (TNF)-alpha antibody.

14. A nucleic acid encoding the humanized antibody or humanized antigen-binding fragment of any one of claims 1 to 8.