

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 humanized antibody or an antigen-binding fragment as described herein for use in therapy.

[0013c] In another aspect, provided herein is the use of the humanized 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 Lane 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.

[0021] FIG. 7 depicts histogram graphs showing the fluorescent staining of 5C3D11 (panel A) and 9E12E5 (panel B) anti-TL1A antibodies on the TL1A expressing HEK293 cell line compared to the untransfected HEK293 cell line.

DESCRIPTION OF THE INVENTION

[0022] Tumor necrosis factor-like protein 1A (TL1A) has been associated with the development and severity of severe colitis and Crohn's Disease. In addition, preclinical and human genetic association data suggests that TL1A is a potential therapeutic target in Crohn's disease. The present disclosure describes neutralizing antibodies against TL1A and offers a novel therapeutic for the treatment of IBD.

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:
 - (a) a heavy chain variable region 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** of SEQ ID NO: 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; and
 - (b) a light chain variable region comprising a light chain complementarity determining region 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: 14;
 - (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.
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 CDR- grafted antibody, a Fab, a Fab', a F(ab')₂, a Fv, a disulfide linked Fv, a scFv, a diabody, a multispecific antibody, a dual specific antibody, a bispecific antibody, or a combination thereof.
3. The humanized antibody or humanized antigen-binding fragment of claim 1 or 2, wherein the humanized 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.

4. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized 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.
5. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized 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.
6. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized 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
7. The humanized antibody or humanized antigen-binding fragment of claim 1, wherein the humanized 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.
8. The humanized antibody or antigen-binding fragment of any one of claims 1-7, for use in therapy.
9. Use of the humanized antibody or antigen-binding fragment of any one of claims 1-7, in the manufacture of a medicament for treating an inflammatory bowel disease in a subject in need thereof.
10. The use of claim 9, wherein the inflammatory bowel disease comprises Crohn's Disease, ulcerative colitis, medically refractory-ulcerative colitis, or a combination thereof.
11. The use of claim 9 or 10, wherein the subject has previously undergone treatment with a second therapeutic agent.

12. The use of claim 11, wherein the second therapeutic agent comprises an anti-tumor necrosis factor (TNF)-alpha antibody.
13. A nucleic acid encoding the humanized antibody or humanized antigen-binding fragment of any one of claims 1 to 7.