

SUMMARY

[0008] This disclosure relates to the development of antigen binding proteins, particularly fully human antibodies that specifically bind TL1A. Preferred antigen binding proteins have strong binding affinity to both human and cynomolgus TL1A, and block TL1A mediated NF-kB activation and T cell activation. These antigen binding proteins have potential to be used as therapeutics for treatment of inflammatory bowel disease (IBD) and other autoimmune and inflammatory conditions.

[0008a] In one aspect, the present disclosure refers to an antigen binding protein specific for TL1A wherein:

the antigen binding protein has a combination of sequences for LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, and HCDR3 selected from the table below:

LCDR1 (SEQ ID NO)	LCDR2 (SEQ ID NO)	LCDR3 (SEQ ID NO)	HCDR1 (SEQ ID NO)	HCDR2 (SEQ ID NO)	HCDR3 (SEQ ID NO)
RASQSVRSSY LA (122)	GASSR AT (124)	QQYGSS PT (126)	GYYW N (188)	EINHAGNTNYPNPS LKS (190)	GYCRSTTCYF DY (192)

[0008b] In another aspect, the present disclosure refers to an antigen binding protein that cross-blocks an antigen binding protein of the disclosure. In yet another aspect, the present disclosure refers to one or more isolated nucleic acids encoding the antigen binding protein of the disclosure. In yet another aspect, the present disclosure refers to one or more expression vectors comprising the nucleic acid or acids of the

disclosure. In a still further aspect, the present disclosure refers to a host cell comprising the one or more expression vectors of the disclosure. In a further aspect, the present disclosure refers to a method for the preparation of an antigen binding protein, comprising a) culturing the host cell of the disclosure under conditions that allow expression of the antigen binding protein; and b) recovering the antigen binding protein from the culture. In a further aspect, the present disclosure refers to a pharmaceutical composition comprising the antigen binding protein of the disclosure and a pharmaceutically acceptable diluent, excipient or carrier. In yet another aspect, the present disclosure refers to the use of the antigen binding protein of the disclosure in the manufacture of a medicament for treating a condition associated with TL1A.

[0009] The disclosure further relates to bispecific antigen binding proteins, particularly bispecific antibodies. Bispecific antigen binding proteins of the disclosure comprise a TL1A binding entity and a TNF- α binding entity. TL1A blocking proteins and TNF- α blocking proteins have different effects in studies measuring inhibition of induction of cytokines IFN γ , IL-5, IL-6, IL-8, and IL-10. TL1A but not TNF- α induces T cell activation in vivo. TL1A and TNF- α induce NF- κ B in different cell types in human peripheral blood monocytes (PBMCs). TL1A and TNF- α further induce different cytokines in human PBMCs. TL1A and TNF- α induce some of the same genes but in different cell types (16 overlapping genes induced by TL1A in whole blood and TNF- α in NCM460 cells; 13 overlapping genes induced by TL1A in whole blood and TNF- α in PBMCs). There is a strong genetic association of TL1A with inflammatory bowel disease (IBD) and anti-TNF agents are clinically validated for treatment of IBD. Such bispecific antigen binding proteins thus are useful for treatment of IBD and other autoimmune and inflammatory conditions. For these and other reasons, there is a benefit to bispecific antigen binding proteins that specifically bind TL1A and TNF- α .

[0010] One format for such bispecific antigen binding proteins is heterodimeric immunoglobulins (hetero Ig). Such hetero Ig antigen binding proteins have one heavy chain-light chain pair directed to TL1A and another directed to TNF- α .

[0011] Another format for such bispecific antigen binding proteins is IgG-scFv molecules. In an IgG-scFv, each heavy chain of an antibody that specifically binds one target is linked to a single chain antibody (scFv) that specifically binds the other target. The scFv portion can be linked to the heavy chain of the IgG portion directly or through a peptide linker. In the IgG-scFv format, the IgG is directed to TL1A and the scFv portion to TNF- α or vice-versa. Bispecific antigen binding proteins in the IgG-scFv format have the advantage of being bivalent for both of their target antigens.

CLAIMS

What is claimed is:

1. An antigen binding protein specific for TL1A wherein:
the antigen binding protein has a combination of sequences for LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, and HCDR3 selected from the table below:

LCDR1 (SEQ ID NO)	LCDR2 (SEQ ID NO)	LCDR3 (SEQ ID NO)	HCDR 1 (SEQ ID NO)	HCDR2 (SEQ ID NO)	HCDR3 (SEQ ID NO)
RASQSVRSSY LA (122)	GASSR AT (124)	QQYGSS PT (126)	GYWW N (188)	EINHAGNTNYP LKS (190)	GYCRSTTCYF DY (192)

2. The antigen binding protein of claim 1, comprising light and heavy chain variable domain sequences of antibody 3B3 (SEQ ID NOS: 22 and 24).
3. The antigen binding protein of claim 1, comprising a combination of light and heavy chain sequences having at least 90% sequence identity with sequences of SEQ ID NOS: 66 and 68.
4. The antigen binding protein of claim 3, comprising light and heavy chain sequences of SEQ ID NOS: 66 and 68.
5. The antigen binding protein of any one of claims 1-4, wherein the antigen binding protein is an antibody.
6. The antigen binding protein of any one of claims 1-4, wherein the antigen binding protein comprises an antibody fragment.
7. An antigen binding protein that cross-blocks an antigen binding protein selected from any one of claims 1-6.

8. One or more isolated nucleic acids encoding the antigen binding protein of any one of claims 1 to 7.
9. One or more expression vectors comprising the nucleic acid or acids of claim 8.
10. A host cell comprising the one or more expression vectors of claim 9.
11. A method for the preparation of an antigen binding protein, comprising:
 - a. culturing the host cell of claim 10 under conditions that allow expression of the antigen binding protein; and
 - b. recovering the antigen binding protein from the culture.
12. A pharmaceutical composition comprising the antigen binding protein of any one of claims 1 to 7 and a pharmaceutically acceptable diluent, excipient or carrier.
13. Use of the antigen binding protein of any one of claims 1 to 7 or the pharmaceutical composition of claim 12 in the manufacture of a medicament for treating a condition associated with TL1A.
14. The use according to claim 13, wherein the condition is inflammatory bowel disease, Crohn's disease, or ulcerative colitis.