

Thus, antagonistic antibodies specific for TIGIT that could inhibit TIGIT receptor activity represent an opportunity to decrease the immunosuppressive effect associated with tumour microenvironments and thereby increase antitumor immune response against tumour cells.

SUMMARY

The present disclosure provides anti-TIGIT antibodies that can decrease the immunosuppressive effect of TIGIT-mediated signalling. In particular, antibodies or antigen binding fragments of the disclosure can inhibit TIGIT-mediated immunosuppression through prevention of ligand binding on T cells (conventional $\alpha\beta$ T cells and non-conventional $\gamma\delta$ T cells) and NK cells and/or depletion of TIGIT positive Treg cells, and/or by inducing internalisation of the TIGIT receptor.

In one aspect, the present disclosure provides an *in vitro* method of promoting T cell activity comprising contacting a population of human $\gamma\delta$ T cells with an antibody or antigen binding fragment thereof which binds to human TIGIT.

In another aspect, the present disclosure provides use of an antibody or antigen binding fragment thereof which binds to human TIGIT in the manufacture of a pharmaceutical composition for promoting T cell activity in a human subject, comprising that a population of human $\gamma\delta$ T cells is to be contacted with the antibody or antigen binding fragment thereof.

In one example, the present disclosure provides an isolated antibody or antigen binding fragment thereof which binds to human TIGIT and which comprises a heavy chain variable domain comprising a heavy chain CDR1 (HCDR1), a heavy chain CDR2 (HCDR2), and a heavy chain CDR3 (HCDR3) selected from the HCDR1, HCDR2 and HCDR3 sequences shown in Figure 1 and which further comprises a light chain variable domain comprising a light chain CDR1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3) selected from the LCDR1, LCDR2, and LCDR3 sequences shown in Figure 2.

In certain examples the antibody or antigen binding fragment comprises a combination of HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein the combination is selected from the group of combinations formed by the HCDRs from each antibody in Figure 1 taken with the LCDRs from the corresponding antibody in Figure 2.

In certain examples, an antibody or antigen binding fragment according to the disclosure may comprise a heavy chain variable domain having an amino acid sequence selected from the group consisting of: SEQ ID Nos: 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 327, 329, and 331 and amino acid sequences exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto; and optionally comprise a light chain variable domain having an amino acid sequence selected from the group consisting of: the amino acid sequences of SEQ ID Nos: 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 328, 330, and 332 and amino acid sequences exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.

In certain examples the antibody or antigen binding fragment comprises a combination of a heavy chain variable domain and a light chain variable domain, wherein the combination is selected from the group of combinations formed by the VH from each antibody in Figure 5, or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto, taken with the VL from the same antibody in Figure 5, or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.

The most-preferred antibodies and antigen binding fragments provided herein are those based on the CDRs or complete variable domains of antibody 31282 provided herein.

As demonstrated herein, these preferred anti-TIGIT antibodies and antigen binding fragments based on antibody 31282 have particularly surprising and advantageous properties. These properties include: a higher affinity for TIGIT expressed on CD8 T cells (from healthy donors or from cancer patients) compared to each previously described anti-TIGIT antibody tested; a better IC₅₀ for competition with CD155/PVR compared to each previously described anti-TIGIT antibody tested; a better EC₅₀ in T cell activation assays compared to each previously described anti-TIGIT antibody tested; and potentially increasing activity in T cells from cancer patient peripheral blood, and importantly in tumour infiltrating lymphocytes. Furthermore, it is surprisingly shown herein that antibodies and antigen binding fragments according to the disclosure, especially those based on antibody 31282, preferentially deplete Treg cells. That is, TIGIT-expressing Treg cells exposed to the provided anti-TIGIT antibodies undergo lysis to a greater proportion compared to conventional CD4 and CD8 T cells. This is surprising because conventional CD4 and CD8 T cells also express TIGIT, but do not undergo cell lysis to the same extent when contacted with the antibodies. It is further surprisingly shown that antibodies and antigen binding fragments according to the disclosure, especially those based on antibody 31282 not only promote conventional T cell pro-inflammatory activity, but also increase activity of non-conventional $\gamma\delta$ T cells.

Thus, in certain preferred examples, provided herein is an antibody or antigen binding fragment comprising HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 wherein:

HCDR1 comprises or consists of SEQ ID NO: 16 (YTFTSYMH),

HCDR2 comprises or consists of SEQ ID NO: 17 (VIGPSGASTSYAQKFQG),

HCDR3 comprises or consists of SEQ ID NO: 18 (ARDHSDYWSGIMEV),

LCDR1 comprises or consists of SEQ ID NO: 61 (RASQSVRSSYLA),

LCDR2 comprises or consists of SEQ ID NO: 62 (GASSRAT), and

LCDR3 comprises or consists of SEQ ID NO: 63 (QQYFSPWT).

In certain such examples, the heavy chain variable domain comprises or consists of an amino acid sequence according to SEQ ID NO: 221 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto, and the light chain variable domain comprises or consists of an amino acid sequence according to SEQ ID NO: 222 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.

In certain preferred examples the anti-TIGIT antibody is antibody 31282 described herein.

In a further example the disclosure provides an isolated antibody or antigen binding fragment thereof, which cross-competes for binding to human TIGIT with an antibody according to the first example of the disclosure, for example an antibody exemplified herein.

In a further example, the disclosure provides an isolated antibody or antigen binding fragment thereof, which binds to the same epitope as an antibody according to the first example of the disclosure, for example an antibody exemplified herein.

In a further example, the disclosure provides an antibody or antigen binding fragment thereof which binds to an epitope of human TIGIT comprising TIGIT residues Q56, and I109, optionally comprising residues Q56, N58 and I109. In preferred examples is provided an antibody or antigen binding fragment thereof which binds to an epitope of human TIGIT comprising TIGIT residues Q56, N58, E60, I68, L73, H76, and I109.

In certain examples, the antibody or antigen binding fragment thereof binds to an epitope of human TIGIT consisting of TIGIT residues Q56, N58, E60, I68, L73, H76, and I109.

In a further example, the disclosure provides an isolated antibody or antigen binding fragment thereof which binds to human TIGIT and which does not compete with CD155 for TIGIT binding.

In certain examples, the antibody or antigen binding fragment which binds to human TIGIT and which does not compete with CD155 for TIGIT binding comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 wherein HCDR1 comprises or consists of SEQ ID NO: 280, HCDR2 comprises or consists of SEQ ID NO: 281, HCDR3 comprises or consists of SEQ ID NO: 282, and LCDR1 comprises or consists of SEQ ID NO: 292, LCDR2 comprises or consists of SEQ ID NO: 293, and LCDR3 comprises or consists of SEQ ID NO: 294.

In certain such examples, the heavy chain variable domain comprises or consists of the amino acid sequence shown as SEQ ID NO: 333 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto, and the light chain variable domain comprises or consists of the amino acid sequence shown as SEQ ID NO: 334 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.

In certain preferred examples, the antibody which binds to human TIGIT and which does not compete with CD155 for TIGIT binding comprises a heavy chain variable domain and a light chain variable domain wherein HCDR1 comprises SEQ ID NO: 353, HCDR2 comprises SEQ ID NO: 354, HCDR3 comprises SEQ ID NO: 355, and LCDR1 comprises SEQ ID NO: 356, LCDR2 comprises SEQ ID NO: 357, and LCDR3 comprises SEQ ID NO: 358.

In certain such examples, the heavy chain variable domain may comprise the amino acid sequence shown as SEQ ID NO: 367 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or

99% sequence identity thereto, and the light chain variable domain may comprise the amino acid sequence shown as SEQ ID NO: 368 or an amino acid sequence exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.

In a further example, the disclosure provides an isolated anti-TIGIT antibody or antigen binding fragment thereof which preferentially depletes TIGIT-expressing Treg cells, optionally wherein the antibody or antigen binding fragment is an antibody or antigen binding fragment according to the first example of the disclosure, for example an antibody exemplified herein..

In a further example the disclosure provides an affinity variant of an antibody according to other examples of the disclosure, for example an antibody exemplified herein.

In a further example the disclosure provides an isolated polynucleotide or combination of isolated polynucleotides encoding an antibody or antigen binding fragment according to any other example of the disclosure, for example an antibody exemplified herein.

In a further example the disclosure provides an isolated polynucleotide encoding a VH and/or a VL domain of an anti-TIGIT antibody, wherein the polynucleotide comprises one or more sequences selected from the group consisting of SEQ ID Nos: 241-270, 335-342 and 369-370.

In a further example the disclosure provides an expression vector comprising a polynucleotide or combination of polynucleotides according to the disclosure operably linked to regulatory sequences which permit expression of the antigen binding polypeptide in a host cell or cell-free expression system.

In a further example the disclosure provides a host cell or cell-free expression system containing an expression vector according to the disclosure.

In a further example the disclosure provides a method of producing a recombinant antibody or antigen binding fragment thereof which comprises culturing a host cell or cell free expression system according to the disclosure under conditions which permit expression of the antibody or antigen binding fragment and recovering the expressed antibody or antigen binding fragment.

In a further example the disclosure provides a pharmaceutical composition comprising an antibody or antigen binding fragment according to the disclosure, for example an antibody exemplified herein, and at least one pharmaceutically acceptable carrier or excipient.

In a further example the disclosure provides an antibody or antigen-binding fragment according to the disclosure or pharmaceutical composition according to the disclosure for use in therapy.

In a further example, the disclosure provides an antibody or antigen-binding fragment according to the disclosure (for example an antibody exemplified herein) or pharmaceutical composition according to the disclosure for use in a method of treating cancer.

In a further example the disclosure provides a method of treating cancer in a subject comprising administering an effective amount of an antibody or antigen-binding fragment according to the disclosure (for example an antibody exemplified herein) or pharmaceutical composition according to the disclosure to the subject, thereby treating the cancer.

In certain preferred examples, the method is a method of treating cancer selected from lung cancer, pancreatic cancer and T-cell lymphoma. In certain preferred examples, the cancer is hepatocellular carcinoma. In certain preferred examples, the cancer is pancreatic adenocarcinoma. In certain preferred examples, the cancer is lung carcinoma. In certain preferred examples, the cancer is Sezary Syndrome.

In a further example, the disclosure provides an antibody or antigen-binding fragment according to the disclosure (for example an antibody exemplified herein) or pharmaceutical composition according to the disclosure for use in a method of treating viral infection, optionally CMV infection.

In a further example is provided a method of treating viral infection in a subject comprising administering an effective amount of an antibody or antigen-binding fragment according to the disclosure or pharmaceutical composition according to the disclosure to the subject, thereby treating the viral infection. In preferred examples the viral infection is CMV infection.

In a further example is provided a method of promoting T cell activity comprising contacting a population of T cells with an antibody or antigen binding fragment according to the disclosure. In certain examples the method promotes $\alpha\beta$ T cell activity. In certain examples the method promotes $\gamma\delta$ T cell activity. In certain examples the method is performed *in vitro*. In certain examples the method is performed *in vivo*, for example in a human subject.

In certain examples is provided a method according to the disclosure, or an antibody or antigen-binding fragment or pharmaceutical composition for use in a method according to the disclosure, wherein the method further comprises administration of one or more additional therapeutic agents. In certain preferred examples, the one or more additional agents are selected from: a chemotherapeutic agent, an anti-PD1 antibody, an anti-PD-L1 antibody, an anti-41BB antibody, an anti-OX40 antibody, an anti-GITR antibody, and an anti-ICOS antibody.

In a further example is provided a combination comprising an anti-TIGIT antibody or antigen binding fragment thereof and one or more of a chemotherapeutic agent, an anti-PD1 antibody, an anti-PD-L1 antibody, an anti-41BB antibody, an anti-OX40 antibody, an anti-GITR antibody, and an anti-ICOS antibody. In a further example is provided a combination according to the disclosure for use in therapy. In a further example is provided a combination according to the disclosure for use in a method of treating cancer or for use in a method of treating viral infection. In a further example is provided a combination according to the disclosure for use in a method according to the disclosure. In

a preferred example the anti-TIGIT antibody or antigen binding fragment thereof is an antibody of the disclosure or an antigen binding fragment thereof.

In a further example is provided a composition or combination for reducing tumor volume. In some examples, the combination further comprises administration of one or more additional therapeutic agents. In certain preferred examples, the one or more additional agents are selected from: a chemotherapeutic agent, an anti-PD1 antibody, an anti-PD-L1 antibody, an anti-41BB antibody, an anti-OX40 antibody, an anti-GITR antibody, and an anti-ICOS antibody.

In a further example is provided a combination comprising an anti-TIGIT antibody or antigen binding fragment thereof according to the disclosure, and a chemotherapeutic agent. In preferred examples the chemotherapeutic agent is doxorubicin. In preferred examples, the combination further comprises an adenosine A2A receptor (A2AR) antagonist. In a further example the combination is provided for use in therapy. In a further example the combination is provided for use in treating cancer. In preferred examples the combination is for use in treating colon carcinoma.

In a further example is provided an anti-TIGIT antibody or antigen binding fragment thereof according to the disclosure for use in a method of treating cancer, wherein the method comprises administering the antibody in combination with a chemotherapeutic agent. In preferred examples, the method further comprises administering an A2AR antagonist, wherein the antibody or antigen binding fragment, the chemotherapeutic agent, and the A2AR antagonist are administered in combination. In preferred examples the cancer is colon carcinoma. In preferred examples the chemotherapeutic agent is doxorubicin. In all relevant examples, it is preferred that any subject to be treated is a human subject. In all relevant examples it is preferred that cells (e.g. T cells) contacted with antibodies according to the disclosure are human cells (e.g. human T cells).

Unless technically incompatible or indicated to the contrary, any preferred example described can optionally be used in combination with one or more of all other preferred examples.

BRIEF DESCRIPTION OF FIGURES

- Figure 1** Table providing heavy chain variable domain (VH) complementarity determining region (CDR) sequences of antibodies of the invention
- Figure 2** Table providing light chain variable domain (VL) CDR sequences of antibodies of the invention
- Figure 3** Table providing heavy chain variable domain (VH) framework (FR) sequences of antibodies of the invention
- Figure 4** Table providing light chain variable domain (VL) framework (FR) sequences of antibodies of the invention
- Figure 5** Table providing heavy chain variable domain (VH) and light chain variable domain (VL) amino acid sequences of antibodies of the invention

- Figure 6** Table providing sequences of polynucleotides encoding VH and VL domains of antibodies according to the invention
- Figure 7** Graph showing the results of a competition assay between hCD155 and anti-TIGIT antibody for binding to Jurkat-hTIGIT
- Figure 8** (A) Graph showing the proportion of TIGIT positive cells within specific T cell populations of PBMC from 7 healthy human donors. (B) Graph showing the

CLAIMS

1. An *in vitro* method of promoting T cell activity comprising contacting a population of human $\gamma\delta$ T cells with an antibody or antigen binding fragment thereof which binds to human TIGIT.
2. Use of an antibody or antigen binding fragment thereof which binds to human TIGIT in the manufacture of a pharmaceutical composition for promoting T cell activity in a human subject, comprising that a population of human $\gamma\delta$ T cells is to be contacted with the antibody or antigen binding fragment thereof.
3. The use according to claim 2, wherein the human subject has cancer.
4. The use according to claim 2, wherein the human subject has a viral infection, optionally wherein the viral infection is a CMV infection.
5. The method according to claim 1, or the use according to any one of claims 2-4, wherein the method or use further comprises that the population of $\gamma\delta$ T cells is to be contacted with one or more of an anti-PD1 antibody, an anti-PD-L1 antibody, an anti-41BB antibody, an anti-OX40 antibody, an anti-GITR antibody, and an anti-ICOS antibody.
6. The method according to claim 1 or 5, or the use according to any one of claims 2-5, wherein the antibody or antigen binding fragment comprises a combination of HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein the combination is selected from the group consisting of:
 - (i) HCDR1 comprising SEQ ID NO:16, HCDR2 comprising SEQ ID NO:17, HCDR3 comprising SEQ ID NO:18, LCDR1 comprising SEQ ID NO:61, LCDR2 comprising SEQ ID NO:62, and LCDR3 comprising SEQ ID NO:63;
 - (ii) HCDR1 comprising SEQ ID NO:4, HCDR2 comprising SEQ ID NO:5, HCDR3 comprising SEQ ID NO:6, LCDR1 comprising SEQ ID NO:49, LCDR2 comprising SEQ ID NO:50, and LCDR3 comprising SEQ ID NO:51;
 - (iii) HCDR1 comprising SEQ ID NO:7, HCDR2 comprising SEQ ID NO:8, HCDR3 comprising SEQ ID NO:9, LCDR1 comprising SEQ ID NO:52, LCDR2 comprising SEQ ID NO:53, and LCDR3 comprising SEQ ID NO:54;
 - (iv) HCDR1 comprising SEQ ID NO:10, HCDR2 comprising SEQ ID NO:11, HCDR3 comprising SEQ ID NO:12, LCDR1 comprising SEQ ID NO:55, LCDR2 comprising SEQ ID NO:56, and LCDR3 comprising SEQ ID NO:57;
 - (v) HCDR1 comprising SEQ ID NO:13, HCDR2 comprising SEQ ID NO:14, HCDR3 comprising SEQ ID NO:15, LCDR1 comprising SEQ ID NO:58, LCDR2 comprising SEQ ID NO:59, and LCDR3 comprising SEQ ID NO:60;
 - (vi) HCDR1 comprising SEQ ID NO:1, HCDR2 comprising SEQ ID NO:2, HCDR3 comprising SEQ ID NO:3, LCDR1 comprising SEQ ID NO:46, LCDR2 comprising SEQ ID NO:47, and LCDR3 comprising SEQ ID NO:48;

- (vii) HCDR1 comprising SEQ ID NO:19, HCDR2 comprising SEQ ID NO:20, HCDR3 comprising SEQ ID NO:21, LCDR1 comprising SEQ ID NO:64, LCDR2 comprising SEQ ID NO:65, and LCDR3 comprising SEQ ID NO:66;
- (viii) HCDR1 comprising SEQ ID NO:22, HCDR2 comprising SEQ ID NO:23, HCDR3 comprising SEQ ID NO:24, LCDR1 comprising SEQ ID NO:67, LCDR2 comprising SEQ ID NO:68, and LCDR3 comprising SEQ ID NO:69;
- (ix) HCDR1 comprising SEQ ID NO:25, HCDR2 comprising SEQ ID NO:26, HCDR3 comprising SEQ ID NO:27, LCDR1 comprising SEQ ID NO:70, LCDR2 comprising SEQ ID NO:71, and LCDR3 comprising SEQ ID NO:72;
- (x) HCDR1 comprising SEQ ID NO:28, HCDR2 comprising SEQ ID NO:29, HCDR3 comprising SEQ ID NO:30, LCDR1 comprising SEQ ID NO:73, LCDR2 comprising SEQ ID NO:74, and LCDR3 comprising SEQ ID NO:75;
- (xi) HCDR1 comprising SEQ ID NO:31, HCDR2 comprising SEQ ID NO:32, HCDR3 comprising SEQ ID NO:33, LCDR1 comprising SEQ ID NO:76, LCDR2 comprising SEQ ID NO:77, and LCDR3 comprising SEQ ID NO:78;
- (xii) HCDR1 comprising SEQ ID NO:34, HCDR2 comprising SEQ ID NO:35, HCDR3 comprising SEQ ID NO:36, LCDR1 comprising SEQ ID NO:79, LCDR2 comprising SEQ ID NO:80, and LCDR3 comprising SEQ ID NO:81;
- (xiii) HCDR1 comprising SEQ ID NO:37, HCDR2 comprising SEQ ID NO:38, HCDR3 comprising SEQ ID NO:39, LCDR1 comprising SEQ ID NO:82, LCDR2 comprising SEQ ID NO:83, and LCDR3 comprising SEQ ID NO:84;
- (xiv) HCDR1 comprising SEQ ID NO:40, HCDR2 comprising SEQ ID NO:41, HCDR3 comprising SEQ ID NO:42, LCDR1 comprising SEQ ID NO:85, LCDR2 comprising SEQ ID NO:86, and LCDR3 comprising SEQ ID NO:87;
- (xv) HCDR1 comprising SEQ ID NO:43, HCDR2 comprising SEQ ID NO:44, HCDR3 comprising SEQ ID NO:45, LCDR1 comprising SEQ ID NO:88, LCDR2 comprising SEQ ID NO:89, and LCDR3 comprising SEQ ID NO:90;
- (xvi) HCDR1 comprising SEQ ID NO:271, HCDR2 comprising SEQ ID NO:272, HCDR3 comprising SEQ ID NO:273, LCDR1 comprising SEQ ID NO:283, LCDR2 comprising SEQ ID NO:284, and LCDR3 comprising SEQ ID NO:285;
- (xvii) HCDR1 comprising SEQ ID NO:274, HCDR2 comprising SEQ ID NO:275, HCDR3 comprising SEQ ID NO:276, LCDR1 comprising SEQ ID NO:286, LCDR2 comprising SEQ ID NO:287, and LCDR3 comprising SEQ ID NO:288;
- (xviii) HCDR1 comprising SEQ ID NO:277, HCDR2 comprising SEQ ID NO:278, HCDR3 comprising SEQ ID NO:279, LCDR1 comprising SEQ ID NO:289, LCDR2 comprising SEQ ID NO:290, and LCDR3 comprising SEQ ID NO:291.

7. The method or the use according to claim 6, wherein the antibody or antigen binding fragment comprises a heavy chain variable domain having an amino acid sequence selected from the group consisting of: SEQ ID Nos: 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 327, 329, and 331, and amino acid sequences exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto; and optionally comprising a light chain variable domain having an amino acid sequence selected from the group consisting of: the amino acid sequences of SEQ ID Nos: 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 328, 330, and 332, and amino acid sequences exhibiting at least 90%, 95%, 97%, 98% or 99% sequence identity thereto.
8. The method or the use according to any one of claims 6 and 7, wherein the antibody or antigen binding fragment comprises a combination of a heavy chain variable domain and a light chain variable domain, wherein the combination is selected from the group consisting of:
 - (i) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:211 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:212 or an amino acid sequence at least 90% identical thereto;
 - (ii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:213 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:214 or an amino acid sequence at least 90% identical thereto;
 - (iii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:215 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:216 or an amino acid sequence at least 90% identical thereto;
 - (iv) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:217 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:218 or an amino acid sequence at least 90% identical thereto;
 - (v) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:219 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:220 or an amino acid sequence at least 90% identical thereto;
 - (vi) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:221 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:222 or an amino acid sequence at least 90% identical thereto;
 - (vii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:223 or an amino acid sequence at least 90% identical thereto and a light chain variable

- domain comprising the amino acid sequence of SEQ ID NO:224 or an amino acid sequence at least 90% identical thereto;
- (viii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:225 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:226 or an amino acid sequence at least 90% identical thereto;
 - (ix) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:227 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:228 or an amino acid sequence at least 90% identical thereto;
 - (x) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:229 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:230 or an amino acid sequence at least 90% identical thereto;
 - (xi) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:231 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:232 or an amino acid sequence at least 90% identical thereto;
 - (xii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:233 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:234 or an amino acid sequence at least 90% identical thereto;
 - (xiii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:235 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:236 or an amino acid sequence at least 90% identical thereto;
 - (xiv) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:237 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:238 or an amino acid sequence at least 90% identical thereto;
 - (xv) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:239 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:240 or an amino acid sequence at least 90% identical thereto;
 - (xvi) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:327 or an amino acid sequence at least 90% identical thereto and a light chain variable

domain comprising the amino acid sequence of SEQ ID NO:328 or an amino acid sequence at least 90% identical thereto;

- (xvii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:329 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:330 or an amino acid sequence at least 90% identical thereto; and

- (xviii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:331 or an amino acid sequence at least 90% identical thereto and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:332 or an amino acid sequence at least 90% identical thereto.

9. The method or the use according to any one of claims 6-8, wherein the antibody or antigen binding fragment comprises:

a heavy chain variable domain comprising a heavy chain CDR1 (HCDR1), a heavy chain CDR2 (HCDR2), and a heavy chain CDR3 (HCDR3), wherein HCDR1 comprises SEQ ID NO: 16, HCDR2 comprises SEQ ID NO: 17, HCDR3 comprises SEQ ID NO: 18;

and which further comprises: a light chain variable domain comprising a light chain CDR1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3), wherein LCDR1 comprises SEQ ID NO: 61, LCDR2 comprises SEQ ID NO: 62, and LCDR3 comprises SEQ ID NO: 63.

10. The method or the use according to any one of claims 6-9, wherein the antibody is a human IgG antibody, preferably a human IgG1 antibody.
11. The method or the use according to any one of claims 6-10, wherein the antibody displays one or more effector functions selected from antibody-dependent cell mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and antibody dependent cell-mediated phagocytosis (ADCP) against cells expressing human TIGIT on the cell surface.