difference in the expression level can result with serious side effects or even abortion of ACT due to non-tolerable toxicity of the treatment.

Additionally, the availability of tumor-specific T cells for efficient tumor cells lysis is dependent on the long-term survival and proliferation capacity of engineered T cells *in vivo*. On the other hand, *in vivo* survival and proliferation of T cells may result with unwanted long-term effects due to the persistence of an uncontrolled CAR-T response (Grupp et al. 2013 N Engl J Med 368(16):1509-18, Maude et al. 2014 2014 N Engl J Med 371(16):1507-17).

One approach for limiting serious treatment-related toxicities and to improve safety of ACT is to restrict the activation and proliferation of CAR-T cells by introducing adaptor molecules in the immunological synapse. Such adaptor molecules comprise small molecular bimodular switches as e.g. recently described folate-FITC switch (Kim et al. J Am Chem Soc 2015; 137:2832-2835). A further approach included artificially modified antibodies comprising a tag to guide and direct the specificity of CAR-T cells to target tumor cells (Ma et al. PNAS 2016; 113(4):E450-458, Cao et al. Angew Chem 2016; 128:1-6, Rogers et al. PNAS 2016; 113(4):E459-468, Tamada et al. Clin Cancer Res 2012; 18(23):6436-6445).

However, existing approaches have several limitations. Immunological synapses relying on molecular switches require introduction of additional elements which might elicit an immune response or result with non-specific off-target effects. Furthermore, the complexity of such multicomponent systems may limit treatment efficacy and tolerability. On the other hand, the introduction of tag structure in existing therapeutic monoclonal antibodies may affect the efficacy and safety profile of these constructs.

Accordingly, the targeted tumor therapy, particularly the adoptive T cell therapy needs to be improved in order to suffice the needs of the cancer patients. Thus, there is still a need to provide improved means having the potential to improve safety and efficacy of ACT and overcome the above disadvantages.

SUMMARY

The present disclosure generally relates to antigen binding receptors capable of specific binding to mutated Fc domains with reduced Fc receptor binding and T cells expressing these antigen binding receptors.

The disclosure relates to an antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is capable of specific binding to a mutated fragment crystallizable (Fc) domain but not capable of specific binding to the non-mutated parent Fc

domain, wherein the mutated Fc domain comprises at least one amino acid substitution compared to the non-mutated parent Fc domain.

In one aspect, the disclosure relates to an antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is capable of specific binding to a mutated fragment crystallizable (Fc) domain but not capable of specific binding to the non-mutated parent Fc domain, wherein the mutated Fc domain comprises at least one amino acid substitution compared to the non-mutated parent Fc domain, wherein the antigen binding moiety is a scFv, a Fab, a crossFab or a scFab.

In one example, Fc receptor binding of the mutated Fc domain is reduced compared to Fc receptor binding of the non-mutated parent Fc domain, particularly wherein the Fc receptor is a Fcγ receptor or neonatal Fc receptor (FcRn). In one example, Fc receptor binding is measured by Surface Plasmon Resonance (SPR) at 25°C.

In one example, the antigen binding moiety is a scFv, a Fab, a crossFab, or a scFab. In a preferred example, the antigen binding moiety is a scFv. In another preferred example, the antigen binding moiety is a Fab or a crossFab.

In one example, the anchoring transmembrane domain is a transmembrane domain selected from the group consisting of the CD8, the CD3z, the FCGR3A, the NKG2D, the CD27, the CD28, the CD137, the OX40, the ICOS, the DAP10 or the DAP12 transmembrane domain or a fragment thereof.

In one example, the anchoring transmembrane domain is the CD28 transmembrane domain, in particular wherein the anchoring transmembrane domain comprises the amino acid sequence of SEQ ID NO:11.

In one example, the antigen binding receptor further comprises at least one stimulatory signaling domain and/or at least one co-stimulatory signaling domain. In one example, the at least one stimulatory signaling domain is individually selected from the group consisting of the intracellular domain of CD3z, of FCGR3A and of NKG2D, or fragments thereof. In one example, the at least one stimulatory signaling domain is a fragment of the intracellular domain of CD3z, in particular wherein the at least one stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:13. In one example, the at least one co-stimulatory signaling domain is individually

selected from the group consisting of the intracellular domain of CD27, of CD28, of CD137, of OX40, of ICOS, of DAP10 and of DAP12, or fragments thereof. In one example, the at least one co-stimulatory signaling domain is a fragment of the CD28 intracellular domain. In one example, the antigen binding receptor comprises one stimulatory signaling domain comprising the intracellular domain of CD3z, or a fragment thereof, and wherein the antigen binding receptor comprises one co-stimulatory signaling domain comprising the intracellular domain of CD28, or a fragment thereof. In one example, the stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:13 and the co-stimulatory signaling domain comprises the amino acid sequence of SEQ ID NO:12.

In one example, the extracellular domain is connected to the anchoring transmembrane domain, optionally through a peptide linker. In one example, the peptide linker comprises the amino acid sequence GGGGS (SEQ ID NO:17). In one example, the anchoring transmembrane domain is connected to a co-signaling domain or to a signaling domain, optionally through a peptide linker. In one example, the signaling and/or co-signaling domains are connected, optionally through at least one peptide linker.

In one example, the antigen binding moiety is a scFv fragment, wherein the scFv fragment is connected at the C-terminus to the N-terminus of the anchoring transmembrane domain, optionally through a peptide linker.

In one example, the antigen binding moiety is a Fab fragment or a crossFab fragment, wherein the Fab or crossFab fragment is connected at the C-terminus of the heavy chain to the N-terminus of the anchoring transmembrane domain, optionally through a peptide linker.

In one example, the antigen binding receptor comprises one co-signaling domain, wherein the co-signaling domain is connected at the N-terminus to the C-terminus of the anchoring transmembrane domain. In one example, the antigen binding receptor comprises one stimulatory signaling domain, wherein the stimulatory signaling domain is connected at the N-terminus to the C-terminus of the co-stimulatory signaling domain.

In one example, the non-mutated parent Fc domain is an IgG1 or an IgG4 Fc domain, particularly a human IgG1 Fc domain. In one example, the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of L234, L235, I253, H310, P331, P329 and H435 according to EU numbering, in particular wherein the amino acid mutation is L234A, L235A, I253A, N297A, H310A, P329G and/or H435A.

In one example, the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of L234, L235 and P329 according to EU numbering, in particular the amino acid mutations L234A, L235A and P329G (“PGLALA”).

In one example, the mutated Fc domain comprises the amino acid mutation P329G according to EU numbering, wherein Fcγ receptor binding of the mutated Fc domain is reduced compared to Fcγ receptor binding of the non-mutated parent Fc domain, in particular wherein the Fcγ receptor is human FcγRIIIa and/or FcγRIIa.

In one example, the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of I253, H310 and H435 according to EU numbering, in particular the amino acid mutations I253A, H310A and H435A ("AAA"), wherein FcRn binding of the mutated Fc domain is reduced compared to FcRn binding of the non-mutated parent Fc domain.

In one example, the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence RYWMN (SEQ ID NO:1);

(b) the CDR H2 amino acid sequence EITPDSSTINYTPSLKD (SEQ ID NO:2); and

(c) the CDR H3 amino acid sequence PYDYGAWFAS (SEQ ID NO:3); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSTGAVTTSNYAN (SEQ ID NO:4);

(e) the CDR L2 amino acid sequence GTNKRAP (SEQ ID NO:5); and

(f) the CDR L3 amino acid sequence ALWYSNHWV (SEQ ID NO:6).

In one example, the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:8 and SEQ ID NO:32, and a light chain variable region (VL) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:9 and SEQ ID NO:33.

In one example, the at least one antigen binding moiety comprises the heavy chain variable region (VH) of SEQ ID NO:8 and the light chain variable region (VL) of SEQ ID NO:9.

In one example, the at least one antigen binding moiety is a scFv capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding receptor comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7 and SEQ ID NO:31. In one example, the antigen binding receptor comprises the amino acid sequence of SEQ ID NO:7.

In one example, the at least one antigen binding moiety is a Fab fragment capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of

specific binding to the non-mutated parent Fc domain, wherein the antigen binding receptor comprises

a) a heavy chain fusion polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:39 and SEQ ID NO:48; and

b) a light chain polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:41 and SEQ ID NO:50.

In one example, the antigen binding receptor comprises

a) the heavy chain fusion polypeptide of SEQ ID NO:39; and

b) the light chain polypeptide of SEQ ID NO:41.

In one example, the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the I253A, H310A and H435A ("AAA") mutations but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence SYGMS (SEQ ID NO:53);

(b) the CDR H2 amino acid sequence SSGGSY (SEQ ID NO:54); and

(c) the CDR H3 amino acid sequence LGMITTGYAMDY (SEQ ID NO:55); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSQTIVHSTGHTYLE (SEQ ID NO:56);

(e) the CDR L2 amino acid sequence KVSNRFS (SEQ ID NO:57); and

(f) the CDR L3 amino acid sequence FQGSHVPYT (SEQ ID NO:58).

In one example, the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the I253A, H310A and H435A ("AAA") mutations but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises a heavy chain variable region (VH) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:61 and a light chain variable region (VL) comprising an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:62.

In one example, the at least one antigen binding moiety comprises

a) the heavy chain variable region (VH) of SEQ ID NO:61; and

b) the light chain variable region (VL) of SEQ ID NO:62.

In one example, the at least one antigen binding moiety is a scFv capable of specific binding to a mutated Fc domain comprising the I253A, H310A and H435A ("AAA") mutations but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding receptor comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:59. In one example, the antigen binding receptor comprises the amino acid sequence of SEQ ID NO:59.

In one example, the at least one antigen binding moiety is a Fab fragment capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding receptor comprises

a) a heavy chain fusion polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:39; and

b) a light chain polypeptide that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO:41.

In one example, the antigen binding receptor comprises

a) the heavy chain fusion polypeptide of SEQ ID NO:39; and

b) the light chain polypeptide of SEQ ID NO:41.

In another aspect, provided is an isolated polynucleotide encoding the antigen binding receptor as described herein. Provided is an isolated polynucleotide encoding a heavy chain fusion polypeptide or a light chain polypeptide of the antigen binding receptor as described herein. Provided is a composition encoding the antigen binding receptor as described herein, comprising a first isolated polynucleotide encoding a heavy chain fusion polypeptide, and a second isolated polynucleotide encoding a light chain polypeptide.

Provided is a polypeptide encoded by the polynucleotide as described herein or by the composition as described herein.

Provided is a vector, particularly an expression vector, comprising the polynucleotide(s) as described herein.

In another aspect, provided is a vector comprising the polynucleotide as described herein. Provided is a transduced T cell comprising the polynucleotide(s) as described herein or the vector as described herein. In another aspect, provided is a transduced T cell capable of expressing the antigen binding receptor as described herein. In

one example, provided is the transduced T cell as described herein, wherein the transduced T cell is co-transduced with a T cell receptor (TCR) capable of specific binding of a target antigen.

In another aspect, provided is a kit comprising

(A) a transduced T cell capable of expressing the antigen binding receptor as described herein; and

(B) an antibody comprising a mutated Fc domain;

wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In another aspect, provided is a kit comprising

(A) an isolated polynucleotide encoding the antigen binding receptor as described herein; and

(B) an antibody comprising a mutated Fc domain;

wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

Provided is a kit comprising

(A) the composition or the vector as described herein encoding the antigen binding receptor as described herein; and

(B) an antibody comprising a mutated Fc domain;

wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In one example, the non-mutated parent Fc domain is an IgG1 or an IgG4 Fc domain, particularly a human IgG1 Fc domain. In one example, provided is a mutated Fc domain comprising at least one amino acid mutation at a position selected from the group consisting of L234, L235, I253, H310, P331, P329 and H435 according to EU numbering, in particular wherein the amino acid mutation is L234A, L235A, I253A, N297A, H310A, P329G and/or H435A. In one example, the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of L234, L235 and P329 according to EU numbering, in particular the amino acid mutations L234A, L235A and P329G (“PGLALA”). In one example, the mutated Fc domain comprises the amino acid mutation P329G according to EU numbering. In one example, the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of I253, H310 and H435 according to EU numbering, in particular the amino acid mutations I253A, H310A and H435A (“AAA”).

In one example, the antibody comprising the mutated Fc domain is capable of specific binding to an antigen on the surface of a tumor cell, in particular wherein the antigen is selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin) and CA-IX, and/or to a peptide bound to a molecule of the human major histocompatibility complex (MHC). In one example, the antibody comprising the mutated Fc domain is capable of specific binding to an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1) and tenascin (TNC).

In another aspect, provided is the kit as described herein for use as a medicament.

In another aspect, provided is the kit as described herein for use in the treatment of a disease.

Provided is the antigen binding receptor or the transduced T cell as described herein for use as a medicament, wherein the transduced T cell expressing the antigen binding receptor is administered before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In another aspect, provided is the transduced T cell as described herein for use as a medicament, wherein a transduced T cell expressing the antigen binding receptor is to be administered before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In one example, provided is the kit as described herein for use in the treatment of a malignant disease. Provided is the antigen binding receptor or the transduced T cell as described herein for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In another aspect, provided is the transduced T cell as described herein for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In one example, said malignant disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

In one example, the transduced T cell is derived from a cell isolated from the subject to be treated. In one example, the transduced T cell is not derived from a cell isolated from the subject to be treated.

Provided is a method of treating a disease in a subject, comprising administering to the subject a transduced T cell capable of expressing the antigen binding receptor as described herein and administering before, simultaneously with or after administration of the transduced T cell a therapeutically effective amount of an antibody comprising a mutated Fc domain, wherein the antigen binding receptor is capable of specific

binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain. In one example, the T cell is additionally isolated from the subject and the transduced T cell is generated by transducing the isolated T cell with the polynucleotide, the composition or the vector as described herein. In one example, the T cell is transduced with a retroviral or lentiviral vector construct or with a non-viral vector construct. In one example, the non-viral vector construct is a sleeping beauty minicircle vector.

In one example, the transduced T cell is administered to the subject by intravenous infusion. In one example, the transduced T cell is contacted with anti-CD3 and/or anti-CD28 antibodies prior to administration to the subject. In one example, the transduced T cell is contacted with at least one cytokine prior to administration to the subject, preferably with interleukin-2 (IL-2), interleukin-7 (IL-7), interleukin-15 (IL-15), and/or interleukin-21, or variants thereof.

In one example, the disease is a malignant disease. In one example, the malignant disease is selected from cancer of epithelial, endothelial or mesothelial origin and cancer of the blood.

In another aspect, provided is a method for inducing lysis of a target cell, comprising contacting the target cell with a transduced T cell capable of expressing the antigen binding receptor as described herein in the presence of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

In one example, the target cell is a cancer cell. In one example, the target cell expresses an antigen selected from the group consisting of FAP, CEA, p95, BCMA, EpCAM, MSLN, MCSP, HER-1, HER-2, HER-3, CD19, CD20, CD22, CD33, CD38, CD52Flt3, FOLR1, Trop-2, CA-12-5, HLA-DR, MUC-1 (mucin), A33-antigen, PSMA, PSCA, transferrin-receptor, TNC (tenascin) and CA-IX. In one example, the target cell expresses an antigen selected from the group consisting of carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), and tenascin (TNC).

In one example, the polynucleotides or the transduced T cell as described herein is used for the manufacture of a medicament. In one example, the medicament is for treatment of a malignant disease.

In another aspect, provided is a use of the transduced T cell as described herein in the manufacture of a medicament for the treatment of a malignant disease.

CLAIMS

1. An antigen binding receptor comprising an anchoring transmembrane domain and an extracellular domain comprising an antigen binding moiety, wherein the antigen binding moiety is capable of specific binding to a mutated fragment crystallizable (Fc) domain but not capable of specific binding to the non-mutated parent Fc domain, wherein the mutated Fc domain comprises at least one amino acid substitution compared to the non-mutated parent Fc domain, wherein the antigen binding moiety is a scFv, a Fab, a crossFab or a scFab.

2. The antigen binding receptor of claim 1, wherein Fc receptor binding of the mutated Fc domain is reduced compared to Fc receptor binding of the non-mutated parent Fc domain.

3. The antigen binding receptor of claim 2, wherein the Fc receptor is a Fcγ receptor or neonatal Fc receptor (FcRn).

4. The antigen binding receptor of any one of claims 1 to 3, wherein the anchoring transmembrane domain is a transmembrane domain selected from the group consisting of the CD8, the CD3z, the FCGR3A, the NKG2D, the CD27, the CD28, the CD137, the OX40, the ICOS, the DAP10 or the DAP12 transmembrane domain.

5. The antigen binding receptor of claim 4, wherein the anchoring transmembrane domain is the CD28 transmembrane domain.

6. The antigen binding receptor of any one of claims 1 to 5 further comprising at least one stimulatory signaling domain and/or at least one co-stimulatory signaling domain.

7. The antigen binding receptor of any one of claims 1 to 6, wherein the at least one stimulatory signaling domain is individually selected from the group consisting of the intracellular domain of CD3z, of FCGR3A and of NKG2D.

8. The antigen binding receptor of claim 7, wherein the at least one stimulatory signaling domain is the CD3z intracellular domain.

9. The antigen binding receptor of any one of claims 1 to 8, wherein the at least one co-stimulatory signaling domain is individually selected from the group consisting of the intracellular domain of CD27, of CD28, of CD137, of OX40, of ICOS, of DAP10 and of DAP12.

10. The antigen binding receptor of claim 9, wherein the at least one co-stimulatory signaling domain is the CD28 intracellular domain.

11. The antigen binding receptor of any one of claims 1 to 10, wherein the antigen binding receptor comprises one stimulatory signaling domain comprising the intracellular domain of CD28, and wherein the antigen binding receptor comprises one co-stimulatory signaling domain comprising the intracellular domain of CD3z.

12. The antigen binding receptor of any one of claims 1 to 11, wherein the antigen binding moiety is a scFv fragment, wherein the scFv fragment is connected at the C-terminus to the N-terminus of the anchoring transmembrane domain.

13. The antigen binding receptor of claim 12, wherein the scFv fragment is connected at the C-terminus to the N-terminus of the anchoring transmembrane domain through a peptide linker.

14. The antigen binding receptor of any one of claims 1 to 13, wherein the antigen binding moiety is a Fab or a crossFab fragment, wherein the Fab or crossFab fragment is connected at the C-terminus of the heavy chain to the N-terminus of the anchoring transmembrane domain.

15. The antigen binding receptor of claim 14, wherein the Fab or crossFab fragment is connected at the C-terminus of the heavy chain to the N-terminus of the anchoring transmembrane domain through a peptide linker.

16. The antigen binding receptor of any one of claims 1 to 15, wherein the mutated Fc domain comprises at least one amino acid mutation at a position selected from the

group consisting of L234, L235, I253, H310, P331, P329 and H435 according to EU numbering.

17. The antigen binding receptor of claim 16, wherein the amino acid mutation is L234A, L235A, I253A, N297A, H310A, P329G and/or H435A.

18. The antigen binding receptor of any one of claims 1 to 17, wherein the mutated Fc domain comprises the amino acid mutation P329G according to EU numbering, wherein Fcγ receptor binding of the mutated Fc domain is reduced compared to Fcγ receptor binding of the non-mutated parent Fc domain.

19. The antigen binding receptor of any one of claims 1 to 17, wherein the mutated Fc domain comprises at least one amino acid mutation at a position selected from the group consisting of I253, H310 and H435 according to EU numbering, wherein FcRn binding of the mutated Fc domain is reduced compared to FcRn binding of the non-mutated parent Fc domain.

20. The antigen binding receptor of claim 19, wherein the mutated Fc domain comprises the amino acid mutations I253A, H310A and H435A ("AAA").

21. The antigen binding receptor of any one of claims 1 to 18, wherein the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the P329G mutation but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence RYWMN (SEQ ID NO:1);

(b) the CDR H2 amino acid sequence EITPDSSTINYTPSLKD (SEQ ID NO:2); and

(c) the CDR H3 amino acid sequence PYDYGAWFAS (SEQ ID NO:3); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSTGAVTTSNYAN (SEQ ID NO:4);

(e) the CDR L2 amino acid sequence GTNKRAP (SEQ ID NO:5); and

(f) the CDR L3 amino acid sequence ALWYSNHWV (SEQ ID NO:6).

22. The antigen binding receptor of any one of claims 1 to 17, 19 or 20, wherein the at least one antigen binding moiety is capable of specific binding to a mutated Fc domain comprising the I253A, H310A and H435A ("AAA") mutations but not capable of specific binding to the non-mutated parent Fc domain, wherein the antigen binding moiety comprises:

(i) a heavy chain variable region (VH) comprising

(a) the heavy chain complementarity-determining region (CDR H) 1 amino acid sequence SYGMS (SEQ ID NO:53);

(b) the CDR H2 amino acid sequence SSGGSY (SEQ ID NO:54); and

(c) the CDR H3 amino acid sequence LGMITTGYAMDY (SEQ ID NO:55); and

(ii) a light chain variable region (VL) comprising

(d) the light chain complementary-determining region (CDR L) 1 amino acid sequence RSSQTIVHSTGHTYLE (SEQ ID NO:56);

(e) the CDR L2 amino acid sequence KVSNRFS (SEQ ID NO:57); and

(f) the CDR L3 amino acid sequence FQGSHVPYT (SEQ ID NO:58).

23. A transduced T cell capable of expressing the antigen binding receptor of any one of claims 1 to 22.

24. An isolated polynucleotide encoding the antigen binding receptor of any one of claims 1 to 22.

25. A vector comprising the polynucleotide of claim 24.

26. The vector of claim 25, wherein the vector is an expression vector.

27. A kit comprising

(A) a transduced T cell capable of expressing the antigen binding receptor of any one of claims 1 to 22; and

(B) an antibody comprising a mutated Fc domain;

wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

28. A kit comprising

(A) an isolated polynucleotide encoding the antigen binding receptor of any one of claims 1 to 22; and

(B) an antibody comprising a mutated Fc domain;

wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

29. The kit of any one of claims 27 or 28, wherein the antibody comprising the mutated Fc domain is capable of specific binding to an antigen selected from the group consisting of fibroblast activation protein (FAP), carcinoembryonic antigen (CEA), mesothelin (MSLN), CD20, folate receptor 1 (FOLR1), and tenascin (TNC).

30. The kit of claim 27 for use as a medicament.

31. The kit of claim 27 for use in the treatment of a disease.

32. The kit for use of claim 31, wherein the disease is a malignant disease.

33. The transduced T cell of claim 23 for use as a medicament, wherein a transduced T cell expressing the antigen binding receptor is to be administered before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

34. The transduced T cell of claim 23 for use in the treatment of a malignant disease, wherein the treatment comprises administration of a transduced T cell expressing the antigen binding receptor before, simultaneously with or after administration of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

35. A method for inducing lysis of a target cell, comprising contacting the target cell with a transduced T cell capable of expressing the antigen binding receptor of any one of claims 1 to 22 in the presence of an antibody comprising a mutated Fc domain wherein the antigen binding receptor is capable of specific binding to the mutated Fc domain but not capable of specific binding to the non-mutated parent Fc domain.

36. Use of the transduced T cell of claim 23 in the manufacture of a medicament for the treatment of a malignant disease.

* * *