

expression of the targeted antigen (targeted tumor antigen) in normal tissues (on-target/off-tumor-reaction; Morgan et al., (2010) *Mol Ther.*, (18) 843-51).

An alternative approach, in which activation of the T cell occurs through a more physiological mechanism, was the provision of an analogous single chain-TCR (scTv)-fragment fused to the C β constant domain derived from the T cell receptor (TCR) and its co-expression with a TCR-derived C α constant domain (Voss et al., (2010) *Blood*, (115) 5154-5163), the latter which recruits the essential endogenous CD3 ζ homodimer (Call et al., (2002) *Cell*, (111) 967-79.). However, in order for these constructs to function as immune system activators, it was essential that their constant domains originate from murine TCRs or need to be murinized (Cohen et al., (2006) *Cancer Res.*, (66) 8878-86; Bialer et al., (2010) *J. Immunol.*, (184) 6232-41) to achieve chain pairing between the scTCR and C α . The fact that these constructs must have xenogenic sequences for functionality raises the risk that the immune system will react against them when administered and impairs or destroys their therapeutic effectiveness.

Thus, there is a need for the provision of alternate recombinant antigen receptors, in which, e.g., the receptor, upon antigen binding, is sufficiently able to activate the T cell in which it is expressed in a normal physiological manner through the endogenous CD3 complex and, optionally, with no requirement for the presence of any amino acid sequences not of human origin, at least in the signal transmission domain of the antigen receptor, that could induce an unwanted immune response against the recombinant antigen receptor itself.

DESCRIPTION OF INVENTION

Summary

The present disclosure relates to recombinant antigen receptors having at least two antigen binding sites. The antigen receptors comprise two peptide chains. The peptide chains each comprise at least two domains, in addition to a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain, in which each of the two domains on one peptide chain forms an antigen binding site with one of the domains on the other peptide chain. In one example, the antigen receptor of the disclosure has the structure of a T cell receptor wherein the chains thereof each comprise said at least two domains forming the antigen binding sites, preferably at the N terminus of the T cell receptor chains.

In one aspect, the present disclosure provides an antigen receptor, which receptor comprises a first peptide chain and a second peptide chain, wherein the first peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain; the second peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain; wherein the first domain from the first peptide chain forms together with one of the domains from the second peptide chain a first antigen binding site, and wherein the second domain from the first peptide chain forms together with the other domain from the second peptide chain a second antigen binding site, wherein (i) the first peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain and the second peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain, or (ii) the first peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain and the second peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain.

In one example, the present disclosure relates to an antigen receptor, which receptor comprises a first peptide chain and a second peptide chain, wherein the first peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain; the second peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain; wherein the first domain from the first peptide chain forms together with one of the domains from the second peptide chain a first antigen binding site, and wherein the second domain from the first peptide chain forms together with the other domain from the second peptide chain a second antigen binding site. In the antigen receptor of this example, the domains forming the respective antigen binding sites are preferably located on different peptide chains. Consequently, antigen binding sites are formed by intermolecular interaction of domains.

In one example, the first and/or second domains each comprise a variable region of an immunoglobulin chain or a variable region of a T cell receptor chain or a portion of the variable region.

In one example, one of the domains forming the first antigen binding site comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen or a portion thereof and the other domain forming the first antigen binding site comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen or a portion thereof. In one example, one of the domains forming the second antigen binding site comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen or a portion thereof and the other domain forming the second antigen binding site comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen or a portion thereof.

In one example, the first domain from the first peptide chain comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen or a portion thereof and the domain from the second peptide chain forming an antigen binding site with the first domain from the first peptide chain comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen or a portion thereof. In one example, the second domain from the first peptide chain comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen or a portion thereof and the domain from the second peptide chain forming an antigen binding site with the second domain from the first peptide chain comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen or a portion thereof.

In one example, the first and the second domains from the first peptide chain each comprise a variable region of a heavy chain of an immunoglobulin or a portion thereof; and the first and the second domains from the second peptide chain each comprise a variable region of a light chain of an immunoglobulin or a portion thereof.

In one example, the N-terminal domain from the first peptide chain forms together with the N-terminal domain from the second peptide chain an antigen binding site; and the C-terminal domain from the first peptide chain forms together with the C-terminal domain from the second peptide chain an antigen binding site.

In one example, the N-terminal domain from the first peptide chain forms together with the C-terminal domain from the second peptide chain an antigen binding site; and the C-terminal domain from the first peptide chain forms together with the N-terminal domain from the second peptide chain an antigen binding site.

In one example of the antigen receptors of the disclosure, the immunoreceptor signal transmission domain comprises a constant or invariant region of a T cell receptor chain or a constant or invariant region of an immune cell Fc receptor chain or a portion of the constant or invariant region. In one example of the antigen receptors of the disclosure, (i) the first peptide chain comprises a variable region of a T cell receptor alpha chain or a portion thereof and a constant region of a T cell receptor alpha chain or a portion thereof and the second peptide chain comprises a variable region of a T cell receptor beta chain or a portion thereof and a constant region of a T cell receptor beta chain or a portion thereof, or (ii) the first peptide chain comprises a variable region of a T cell receptor beta chain or a portion thereof and a constant region of a T cell receptor beta chain or a portion thereof and the second peptide chain comprises a variable region of a T cell receptor alpha chain or a portion thereof and a constant region of a T cell receptor alpha chain or a portion thereof. In this example, the variable region of a T cell receptor alpha chain or a portion thereof and the constant region of a T cell receptor alpha chain or a portion thereof corresponds or essentially corresponds to the alpha chain of a T cell receptor, and the variable region of a T cell receptor beta chain or a portion thereof and the constant region of a T cell receptor beta chain or a portion thereof corresponds or essentially corresponds to the beta chain of a T cell receptor, preferably the same T cell receptor from which the alpha chain of a T cell receptor is derived. The domains forming the antigen binding sites are preferably fused at the N terminus of the chains, optionally separated by a linker.

In one example of the antigen receptors of the disclosure, the variable region of a T cell receptor chain or a portion thereof, and/or the immunoreceptor signal transmission domain such as the constant region of a T cell receptor or a portion thereof is of human origin. Thus, the chain of a T cell receptor to which the variable region of a T cell receptor chain or a portion thereof and the constant region of a T cell receptor chain or a portion thereof may correspond or essentially correspond may be of human origin.

In one example, an antigen receptor of the disclosure comprises (a) linker(s) connecting domains of the antigen receptor. In one example, an antigen receptor of the disclosure comprises one or more linkers between the domains forming the antigen binding sites and/or between the domains forming the antigen binding sites and the variable regions of a T cell receptor chain or a portion thereof. The linker can be an arbitrary amino acid sequence of any length so long as it does not interfere with the functions of the antigen receptor, such as the ability of the antigen receptor to

bind antigen or to associate with the endogenous CD3 complex, or interfere with the ability of the antigen receptor to induce an immune response upon antigen binding.

In one example of the antigen receptors of the disclosure, the first and second antigen binding sites bind to the same antigen or different antigens. In one example of the antigen receptors of the disclosure, the first and second antigen binding sites bind to different epitopes on the same antigen. Consequently, while the domains forming the first antigen binding site are preferably derived from the same immunoglobulin and the domains forming the second antigen binding site are preferably derived from the same immunoglobulin, the domains forming the first antigen binding site and the domains forming the second antigen binding site are derived from the same or different immunoglobulins, said different immunoglobulins binding to the same or different antigens.

In one example, the antigen is a disease-specific antigen, preferably a tumor antigen. In one example, the antigen is expressed on the surface of a cell.

In one example, the present disclosure relates to a peptide chain of the antigen receptors of the disclosure. In one example, the present disclosure relates to a peptide chain comprising a first and a second domain which each comprise a variable region of a heavy chain of an immunoglobulin or a portion thereof or each comprise a variable region of a light chain of an immunoglobulin or a portion thereof and wherein the peptide chain further comprises a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain such as a constant region of a T cell receptor chain or a portion thereof. Further examples of the peptide chains of the disclosure are as described herein for the antigen receptors of the disclosure.

In another aspect, the present disclosure provides a recombinant cell expressing the first peptide chain, the second peptide chain or both the first and second peptide chains defined herein. In one example, the present disclosure relates to a cell, in particular an immune effector cell such as a T cell, genetically modified to express an antigen receptor of the disclosure. In one example, the present disclosure relates to a recombinant cell, in particular an immune effector cell such as a T cell, expressing the first peptide chain, the second peptide chain or both the first and second peptide chains of an antigen receptor of the disclosure or expressing a peptide chain of the disclosure. Further examples of the cell or recombinant cell of the disclosure are as described herein for the antigen receptors of the disclosure or the peptide chains of the disclosure.

In yet another aspect, the present disclosure provides a method for producing a cell expressing an antigen receptor which receptor comprises a first peptide chain and a second peptide chain, the method comprising: (a) providing a cell; (b) providing a first genetic construct encoding the first peptide chain comprising at least a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain; (c) providing a second genetic construct encoding the second peptide chain comprising at least a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain; (d) introducing the first and second genetic constructs into the cell; and (e) allowing the constructs to be expressed in the cell; wherein the first domain from the first peptide chain is able to form together with one of the domains from the second peptide chain a first antigen binding site, and wherein the second domain from the first peptide chain is able to form together with the other domain from the second peptide chain a second antigen binding site; wherein (i) the first peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain and the second peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain, or (ii) the first peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain and the second peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain.

In one example, the present disclosure relates to a method for producing a cell expressing an antigen receptor of the disclosure, the method comprising: (a) providing a cell; (b) providing a first genetic construct encoding the first peptide chain of an antigen receptor of the disclosure; (c) providing a second genetic construct encoding the second peptide chain of an antigen receptor of the disclosure; (d) introducing the first and second genetic constructs into the cell; and (e) allowing the constructs to be expressed in the cell. In one example, the present disclosure relates to a method for producing a cell expressing an antigen receptor which receptor comprises a first peptide chain and a second peptide chain, the method comprising: (a) providing a cell; (b) providing a first genetic construct encoding the first peptide chain comprising a first domain, a second domain, a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain; (c) providing a second genetic construct encoding the second peptide chain comprising at least a first domain, a second domain, a variable region of a T cell receptor chain or a portion thereof, and an immunoreceptor signal transmission domain; (d) introducing the first and second genetic constructs into the cell; and (e) allowing the constructs to be expressed in the cell; wherein the first domain from the first peptide chain is able to form together with one of the

domains from the second peptide chain a first antigen binding site, and wherein the second domain from the first peptide chain is able to form together with the other domain from the second peptide chain a second antigen binding site. In one example of the methods of the disclosure, expression of the antigen receptor is at the cell surface. In one example of the methods of the disclosure, the first peptide chain and the second peptide chain are provided on a single genetic construct. In one example of the methods of the disclosure, the cell is a human cell. In one example of the methods of the disclosure, the cell is an immune effector cell such as a T cell. In one example of the methods of the disclosure, the genetic constructs comprise DNA and/or RNA. Further examples of the methods of the disclosure are as described herein for the antigen receptors of the disclosure.

In another aspect, the present disclosure provides a recombinant cell produced by the method of as described herein, wherein said cell is preferably a human cell. In one example, the present disclosure relates to a recombinant cell, in particular an immune effector cell such as a T cell, produced by the methods of the disclosure for producing a cell expressing an antigen receptor. Further examples of the recombinant cell of the disclosure are as described herein for the antigen receptors of the disclosure or the methods of the disclosure for producing a cell expressing an antigen receptor.

In another aspect, the present disclosure provides a nucleic acid encoding the first peptide chain, the second peptide chain or both the first and second peptide chains defined herein, which is preferably DNA or RNA. In one example, the present disclosure relates to a nucleic acid such as DNA or RNA encoding the first peptide chain, the second peptide chain or both the first and second peptide chains of an antigen receptor of the disclosure or encoding a peptide chain of the disclosure. Further examples of the nucleic acid of the disclosure are as described herein for the antigen receptors of the disclosure or the peptide chains of the disclosure.

The present disclosure generally embraces the treatment of diseases by targeting cells expressing one or more antigens on the cell surface such as diseased cells expressing one or more disease-specific antigens on the cell surface, in particular cancer cells expressing one or more tumor antigens on the cell surface using antigen receptors of the disclosure. The methods provide for the selective eradication of cells that express on their surface one or more antigens, thereby minimizing adverse effects to normal cells not expressing the antigen(s). In one example, T cells genetically modified to express an antigen receptor of the disclosure targeting the cells through binding to the antigen(s) are administered. T cells are able to recognize diseased cells expressing the antigen(s)

on the cell surface, resulting in the eradication of diseased cells. In one example, the target cell population or target tissue is tumor cells or tumor tissue.

In a further aspect, the present disclosure provides a pharmaceutical composition comprising the antigen receptor as described herein, the recombinant cell as described herein, or the nucleic acid as described herein; and a pharmaceutically acceptable carrier, optionally for use as a medicament. In one example, the present disclosure relates to a pharmaceutical composition comprising the antigen receptor of the disclosure, the recombinant cell of the disclosure, or the nucleic acid of the disclosure; and a pharmaceutically acceptable carrier. The pharmaceutical composition of the disclosure may be used as a medicament, in particular in the treatment of a disease such as cancer characterized by expression of one or more antigens which are bound by the antigen receptor of the disclosure such as one or more tumor antigens.

In a further aspect, the present disclosure provides use of the pharmaceutical composition as described herein in the manufacture of a medicament for treating a disease characterized by expression of at least one antigen which is bound by the antigen receptor, wherein the antigen is preferably a tumor antigen. In one example, the present disclosure relates to a method of treating a disease such as cancer comprising administering to a subject a therapeutically effective amount of the pharmaceutical composition of the disclosure, wherein the disease is characterized by expression of at least one antigen such as a tumor antigen which is bound by the antigen receptor.

In a further aspect, the present disclosure provides use of the antigen receptor as described herein, recombinant cell as described herein, or nucleic acid as described herein in the manufacture of a medicament for treating a disease, wherein the disease is characterized by expression of at least one antigen which is bound by the antigen receptor and wherein the disease is preferably cancer. In one example, the present disclosure relates to a method of treating a subject having a disease, disorder or condition associated with expression or elevated expression of at least one antigen, the method comprising administering to the subject T cells genetically modified to express an antigen receptor of the disclosure targeted to the at least one antigen. In one example, the disease, disorder or condition is cancer. In one example, the T cells may be autologous, allogeneic or syngeneic to the subject.

In one example of the disclosure, the antigen receptor binds to only one antigen (e.g. by being monospecific and recognizing the same epitope or by being bispecific or multispecific and

recognizing different epitopes on the same antigen) or binds to different antigens, in particular two different antigens.

In one example of all examples of the disclosure, the method of treating further comprises obtaining a sample of cells from a subject, the sample comprising T cells or T cell progenitors, and transfecting the cells with a nucleic acid encoding the antigen receptor of the disclosure to provide T cells genetically modified to express the antigen receptor. In one example of all examples of the disclosure, the T cells genetically modified to express the antigen receptor are stably or transiently transfected with nucleic acid encoding the antigen receptor. Thus, the nucleic acid encoding the antigen receptor is integrated or not integrated into the genome of the T cells. In one example of all examples of the disclosure, the T cells and/or the sample of cells are from the subject to which the T cells genetically modified to express the antigen receptor are administered. In one example of all examples of the disclosure, the T cells and/or the sample of cells are from a mammal which is different to the mammal to which the T cells genetically modified to express the antigen receptor are administered.

In one example of all examples of the disclosure, the T cells genetically modified to express the antigen receptor are inactivated for expression of an endogenous T cell receptor and/or endogenous HLA.

In one example of all examples of the disclosure, an antigen is expressed in a diseased cell such as a cancer cell. In one example, an antigen is expressed on the surface of a diseased cell such as a cancer cell. In one example, an antigen receptor binds to an extracellular domain or to an epitope in an extracellular domain of an antigen. In one example, an antigen receptor binds to native epitopes of an antigen present on the surface of living cells. In one example of all examples of the disclosure, the antigen is a tumor antigen. In one example of all examples of the disclosure, the antigen is selected from the group consisting of claudins, such as claudin 6 and claudin 18.2, CD19, CD20, CD22, CD33, CD123, mesothelin, CEA, c-Met, PSMA, GD-2, and NY-ESO-1. In one example of all examples of the disclosure, the antigen is a pathogen antigen. The pathogen may be a fungal, viral, or bacterial pathogen. In one example of all examples of the disclosure, expression of the antigen is at the cell surface. In one example an antigen is a claudin, in particular claudin 6 or claudin 18.2, and said antigen receptor binds to the first extracellular loop of said claudin. In one example, binding of said antigen receptor when expressed by T cells and/or present on T cells to an antigen present on cells results in immune effector functions of said T cells such as the release

of cytokines. In one example, binding of said antigen receptor when expressed by T cells and/or present on T cells to an antigen present on cells such as antigen presenting cells results in stimulation, priming and/or expansion of said T cells. In one example, binding of said antigen receptor when expressed by T cells and/or present on T cells to an antigen present on diseased cells such as cancer cells results in cytolysis and/or apoptosis of the diseased cells, wherein said T cells preferably release cytotoxic factors, e.g. perforins and granzymes.

In one example of all examples of the disclosure, the domains of an antigen receptor forming antigen binding sites are comprised by an ectodomain of the antigen receptor. In one example of all examples of the disclosure, an antigen receptor of the disclosure comprises a transmembrane domain. In one example, the transmembrane domain is a hydrophobic alpha helix that spans the membrane.

In one example of all examples of the disclosure, an antigen receptor of the disclosure comprises a signal peptide which directs the nascent protein into the endoplasmic reticulum. In one example, the signal peptide precedes the domains forming antigen binding sites.

In one example of all examples of the disclosure, an antigen receptor of the disclosure is preferably specific for the antigen to which it is targeted, in particular when present on the surface of a cell such as a diseased cell or an antigen-presenting cell.

In one example of all examples of the disclosure, an antigen receptor of the disclosure may be expressed by and/or present on the surface of an immunoreactive cell, such as a T cell, preferably a cytotoxic T cell. In one example, the T cell is reactive with the antigen(s) to which the an antigen receptor of the disclosure is targeted.

In a further example, the disclosure provides the agents and compositions described herein for use in the methods described herein.

Other features and advantages of the instant disclosure will be apparent from the following detailed description and claims.

Detailed description of the invention

Although the present invention is described in detail below, it is to be understood that this invention is not limited to the particular methodologies, protocols and reagents described herein as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art.

In the following, the elements of the present invention will be described. These elements are listed with specific embodiments, however, it should be understood that they may be combined

CLAIMS

1. An antigen receptor, which receptor comprises a first peptide chain and a second peptide chain,
wherein

the first peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain;

the second peptide chain comprises a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain;

wherein the first domain from the first peptide chain forms together with one of the domains from the second peptide chain a first antigen binding site, and

wherein the second domain from the first peptide chain forms together with the other domain from the second peptide chain a second antigen binding site, wherein

(i) the first peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain and the second peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain, or

(ii) the first peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain and the second peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain.

2. The receptor of claim 1, wherein the first and/or second peptide chains further comprise a linker between the first and second domains and/or between the first and second domains and the variable region of a T cell receptor chain, wherein the linker is preferably an arbitrary amino acid sequence.

3. The receptor of claim 1 or 2, wherein the first and/or second domains each comprise a variable region of an immunoglobulin chain or a variable region of a T cell receptor chain.

4. The receptor of any one of claims 1 to 3, wherein the first domain from the first peptide chain comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen and the domain from the second peptide chain forming an antigen

binding site with the first domain from the first peptide chain comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen.

5. The receptor of any one of claims 1 to 4, wherein the second domain from the first peptide chain comprises a variable region of a heavy chain of an immunoglobulin with a specificity for an antigen and the domain from the second peptide chain forming an antigen binding site with the second domain from the first peptide chain comprises a variable region of a light chain of an immunoglobulin with a specificity for the antigen.

6. The receptor of any one of claims 1 to 5, wherein
the first and the second domains from the first peptide chain each comprise a variable region of a heavy chain of an immunoglobulin; and
the first and the second domains from the second peptide chain each comprise a variable region of a light chain of an immunoglobulin.

7. The receptor of any one of claims 1 to 6, wherein
the N-terminal domain from the first peptide chain forms together with the N-terminal domain from the second peptide chain an antigen binding site; and
the C-terminal domain from the first peptide chain forms together with the C-terminal domain from the second peptide chain an antigen binding site.

8. A recombinant cell expressing the first peptide chain, the second peptide chain or both the first and second peptide chains defined in any one of claims 1 to 7.

9. A method for producing a cell expressing an antigen receptor which receptor comprises a first peptide chain and a second peptide chain, the method comprising:

- (a) providing a cell;
- (b) providing a first genetic construct encoding the first peptide chain comprising at least a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain;
- (c) providing a second genetic construct encoding the second peptide chain comprising at least a first domain, a second domain, a variable region of a T cell receptor chain, and an immunoreceptor signal transmission domain;
- (d) introducing the first and second genetic constructs into the cell; and

(e) allowing the constructs to be expressed in the cell;

wherein the first domain from the first peptide chain is able to form together with one of the domains from the second peptide chain a first antigen binding site, and

wherein the second domain from the first peptide chain is able to form together with the other domain from the second peptide chain a second antigen binding site;
wherein

(i) the first peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain and the second peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain, or

(ii) the first peptide chain comprises a variable region of a T cell receptor beta chain and a constant region of a T cell receptor beta chain and the second peptide chain comprises a variable region of a T cell receptor alpha chain and a constant region of a T cell receptor alpha chain.

10. The method of claim 9, wherein the first peptide chain and the second peptide chain are provided on a single genetic construct.

11. The method of claim 9 or 10, wherein the cell is a human cell, preferably a T cell.

12. A recombinant cell produced by the method of any one of claims 9 to 11, wherein said cell is preferably a human cell.

13. A nucleic acid encoding the first peptide chain, the second peptide chain or both the first and second peptide chains defined in any one of claims 1 to 7, which is preferably DNA or RNA.

14. A pharmaceutical composition comprising the antigen receptor of any one of claims 1 to 7, the recombinant cell of claim 8 or 12, or the nucleic acid of claim 13; and a pharmaceutically acceptable carrier, optionally for use as a medicament.

15. Use of the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating a disease characterized by expression of at least one antigen which is bound by the antigen receptor, wherein the antigen is preferably a tumor antigen.

16. The use of claim 15, wherein the disease is cancer.

17. Use of the antigen receptor of any one of claims 1 to 7, recombinant cell of claim 8 or 12, or nucleic acid of claim 13 in the manufacture of a medicament for treating a disease, wherein the disease is characterized by expression of at least one antigen which is bound by the antigen receptor and wherein the disease is preferably cancer.