

Claims

1. A modified T cell receptor (TCR) α or β chain,
 - (i) that maintains the ability to bind to an antigen-MHC complex, and
 - 5 (ii) wherein the α chain comprises a variable domain comprising at least the framework region (FR) 1 to 3 having at least 95 % sequence identity with SEQ ID NO: 1 or 3; and/or
 - (iii) wherein the β chain comprises a variable domain comprising at least the framework region (FR) 1 to 3 having at least 95 % sequence identity with SEQ ID NO: 2 or 4; and
 - 10 (iv) wherein the amino acid at position 44 according to the IMGT numbering of a non-modified α and/or β chain is substituted by an amino acid selected from the group consisting of the amino acids R, D, E, K, L, W, and V that reduces the pairing of said modified α and/or β chain with a non-modified α or β chain.

- 15 2. A recombinant T cell receptor (TCR) heterodimer comprising a modified α chain and/or a modified β chain, wherein said TCR maintains the ability to bind to an antigen-MHC complex, wherein said modification of the α and/or β chain thereof is selected from a substitution of position 44 according to the IMGT numbering of a non-modified α and/or β chain by an amino acid selected from the group consisting of R, D, E, K, L, W, and V that reduces the pairing of said modified α and/or β chain with a non-modified α or β chain.

- 20 3. The recombinant T cell receptor (TCR) heterodimer according to claim 2, wherein the modified α chain has a variable domain sequence comprising at least the framework regions of a sequence having at least 95 % sequence identity with SEQ ID NO: 1 or 3; and/or wherein the modified β chain has a variable domain sequence comprising the framework regions of a sequence having at least 95 % sequence identity with SEQ ID NO 2 or 4.

- 30 4. The recombinant T cell receptor (TCR) heterodimer according to claim 2 or 3, wherein said modification of the α and β chain is selected from a substitution pair of the group consisting of α Q44D / β Q44R; α Q44R / β Q44D; α Q44E / β Q44K; α Q44K / β Q44E; α Q44D / β Q44K; α Q44K / β Q44D; α Q44E / β Q44R; α Q44R / β Q44E; α Q44L / β Q44W; α Q44W / β Q44L; α Q44V / β Q44W; α Q44W / β Q44V; α W44D / β Q44R; α W44R / β Q44D; α W44E / β Q44K; α W44K / β Q44E; α W44D / β Q44K; α W44K / β Q44D; α W44E / β Q44R; α W44R / β Q44E; α W44L / β Q44W; α W44 / β Q44L; α W44V / β Q44W; α W44 / β Q44V; α H44D / β Q44R; α H44R / β Q44D; α H44E / β Q44K; α H44K / β Q44E; α H44D / β Q44K; α H44K / β Q44D; α H44E / β Q44R; α H44R / β Q44E; α H44L / β Q44W; α H44W / β Q44L; α H44V / β Q44W; α H44W / β Q44V; α K44D /
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- β Q44R; α K44R / β Q44D; α K44E / β Q44K; α K44 / β Q44E; α K44D / β Q44K; α K44 / β Q44D;
 α K44E / β Q44R; α K44R / β Q44E; α K44L / β Q44W; α K44W / β Q44L; α K44V / β Q44W; α K44W
/ β Q44V; α E44D / β Q44R; α E44R / β Q44D; α E44 / β Q44K; α E44K / β Q44E; α E44D / β Q44K;
 α E44K / β Q44D; α E44 / β Q44R; α E44R / β Q44E; α E44L / β Q44W; α E44W / β Q44L; α E44V /
5 β Q44W; α E44W / β Q44V; α Q44D / β R44 ; α Q44R / β R44D; α Q44E / β R44K; α Q44K / β R44E;
 α Q44D / β R44K; α Q44K / β R44D; α Q44E / β R44 ; α Q44R / β R44E; α Q44L / β R44W; α Q44W
/ β R44L; α Q44V / β R44W; α Q44W / β R44V; α W44D / β R44; α W44R / β R44D; α W44E /
 β R44K; α W44K / β R44E; α W44D / β R44K; α W44K / β R44D; α W44E / β R44 ; α W44R / β R44E;
 α W44L / β R44W; α W44 / β R44L; α W44V / β R44W; α W44 / β R44V; α H44D / β R44 ; α H44R
10 / β R44D; α H44E / β R44K; α H44K / β R44E; α H44D / β R44K; α H44K / β R44D; α H44E / β R44 ;
 α H44R / β R44E; α H44L / β R44W; α H44W / β R44L; α H44V / β R44W; α H44W / β R44V; α K44D
/ β R44 ; α K44R / β R44D; α K44E / β R44K; α K44 / β R44E; α K44D / β R44K; α K44 / β R44D;
 α K44E / β R44 ; α K44R / β R44E; α K44L / β R44W; α K44W / β R44L; α K44V / β R44W; α K44W
/ β R44V; α E44D / β R44 ; α E44R / β R44D; α E44 / β R44K; α E44K / β R44E; α E44D / β R44K;
15 α E44K / β R44D; α E44R / β R44E; α E44L / β R44W; α E44W / β R44L; α E44V / β R44W; and
 α E44W / β R44V, preferably selected from the group consisting of α 44D / β 44R; α 44R / β 44D;
 α 44E / β 44K; α 44K / β 44E; α 44D / β 44K; α 44K / β 44D; α 44E / β 44R; and α 44R / β 44E.
5. The recombinant T cell receptor (TCR) heterodimer according to any one of claims 2 to 4, wherein
20 said α chain of the TCR has a variable domain sequence comprising at least the framework regions
of a sequence having at least 95 % sequence identity with SEQ ID NO: 1 or 3, and/or the β chain
of the TCR has a variable domain sequence comprising the framework regions of a sequence
having at least 95 % sequence identity with SEQ ID NO: 2 or 4.
- 25 6. A nucleic acid molecule encoding a modified T cell receptor (TCR) α or β chain according to
claim 1, and/or a recombinant T cell receptor (TCR) heterodimer according to any one of claims
2 to 5.
- 30 7. A plasmid or expression vector comprising at least one of the nucleic acid molecules according
to claim 6.
8. An *in vitro* method of preparing a modified T cell, said method comprising transducing or
transfecting a T cell obtained from a subject with one or more nucleic acid molecules according
to claim 6, or a plasmid or expression vector according to claim 7.
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9. A modified T cell produced according to claim 8.

10. The modified T cell according to claim 9 for use in an autologous T cell treatment of a subject in need thereof.
- 5 11. The modified T cell according to claim 9 for use in the treatment of a subject in need of said treatment that is suffering from or is at risk of developing, and/or is diagnosed with a neoplastic, inflammatory, infectious or autoimmune disease, wherein a preparation comprising said modified T cell is to be administered to said subject in need thereof.
- 10 12. Use of the modified T cell according to claim 9 in the manufacture of a medicament for the treatment of a neoplastic, inflammatory, infectious or autoimmune disease.
13. The recombinant T cell receptor (TCR) heterodimer according to any one of claims 2 to 5, wherein said TCR specifically binds to an antigen presented by an MHC complex, wherein said antigen is
15 selected from an epitope of a tumor associated antigen (TAA).