

Claims:

Claim 1. A Fc fusion protein for use in the treatment of a cancer, wherein said Fc fusion protein is a homodimer of two polypeptides, each comprising (i) a non-cytolytic immunoglobulin IgG Fc domain and (ii) a heterologous polypeptide comprising a sequence of a human IL-10 as set forth in **SEQ ID NO: 1** or a variant thereof having deletions and/or conservative substitutions of 1, 2, 3, 4, 5 or 6 amino acid residues, wherein the heterologous polypeptide is covalently linked to the N-terminus or the C-terminus of the Fc domain by a polypeptide linker that is a flexible hinge selected from SEQ ID NO: 3, SEQ ID NO: 6 and a sequence of a GS linker and the two heterologous polypeptides are non-covalently assembled in a homodimer; and

wherein the immunoglobulin non-cytolytic IgG1 Fc domain is selected from the group consisting of, or comprising:

i) a non-cytolytic IgG1 Fc comprising a sequence of **SEQ ID NO: 2** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues;

ii) a non-cytolytic IgG2 Fc fragment comprising a sequence of **SEQ ID NO: 5** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues,

iii) a non-cytolytic IgG3 Fc fragment comprising a sequence of **SEQ ID NO: 8** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues, and

iv) a non-cytolytic IgG4 Fc fragment comprising a sequence of **SEQ ID NO: 11** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

Claim 2. The fusion protein for use according to claim 1, wherein the sequence of said fusion protein comprises a sequence of **SEQ ID NO: 4** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

Claim 3. The fusion protein for use according to any one of claims 1 or 2, wherein the sequence of said fusion protein comprises a sequence of **SEQ ID NO: 7** or a variant thereof

comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

5 Claim 4. The fusion protein for use according to claim 1, wherein the sequence of said fusion protein comprises a sequence of **SEQ ID NO: 10** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

Claim 5. The fusion protein for use according to claim 1, wherein the sequence of said fusion protein comprises a sequence of **SEQ ID NO: 13** or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

10 Claim 6. Use of fusion protein of any one claims 1 to 5 in the manufacture of a medicament for the treatment of a cancer.

Claim 7. The use according to claim 6, wherein said use in the treatment of a cancer is anti-cancer immunotherapy.

Claim 8. The use according to claim 7, wherein said anticancer immunotherapy is selected from Adoptive Cell Therapy (ACT) or immune checkpoint blockade therapy.

15 Claim 9. The use according to claim 8, wherein ACT is selected from TCR-T, CAR-T or TILs therapies.

20 Claim 10. The use according to any one of claims 6 to 9, wherein said cancer is a solid tumor cancer, such as lung cancer, breast cancer, ovarian cancer, cervical cancer, uterus cancer, head and neck cancer, glioblastoma, hepatocellular carcinoma, colon cancer, rectal cancer, colorectal carcinoma, kidney cancer, prostate cancer, gastric cancer, bronchus cancer, pancreatic cancer, urinary bladder cancer, hepatic cancer and brain cancer or skin cancer, in particular melanoma.

25 Claim 11. A pharmaceutical composition comprising at least one Fc fusion protein, wherein said Fc fusion protein is a homodimer of two polypeptides, each comprising a non-cytolytic immunoglobulin IgG Fc domain and (ii) a heterologous polypeptide comprising a sequence of a human IL-10 as set forth in **SEQ ID NO: 1** or a variant thereof having deletions and/or conservative substitutions of 1, 2, 3, 4, 5 or 6 amino acid residues,

wherein the heterologous polypeptide is covalently linked to the N-terminus or the C-terminus of the Fc domain by a polypeptide linker that is a flexible hinge selected from **SEQ ID NO: 3, SEQ ID NO: 6** and a sequence of a GS linker and the two heterologous polypeptides are non-covalently assembled in a homodimer,

5 and wherein the immunoglobulin non-cytolytic IgG Fc domain is selected from the group consisting in, or comprising,

i) a non-cytolytic IgG1 Fc fragment comprising a sequence of SEQ ID NO: 2 or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues,

10 ii) a non-cytolytic IgG2 Fc fragment comprising a sequence of SEQ ID NO: 5 or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues,

iii) a non-cytolytic IgG3 Fc fragment comprising a sequence of SEQ ID NO: 8 or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues, and

15 iv) a non-cytolytic IgG4 Fc fragment comprising a sequence of SEQ ID NO: 11 or a variant thereof comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues and

a pharmaceutically acceptable carrier, diluent or excipient thereof and at least one anti-cancer immunotherapy agent.

20 Claim 12. The pharmaceutical composition according to claim 11, wherein the sequence of said Fc fusion protein comprises a sequence of **SEQ ID NO: 4, SEQ ID NO:7, SEQ ID NO:10, SEQ ID NO:13** or a variant of any of these sequences comprising deletions and/or conservative substitutions of 1, 2, 3, 4, or 5 amino acid residues.

25 Claim13. Use of the pharmaceutical composition according to claims 11 or 12 for in the preparation of a medicament for the treatment of cancer, in particular ACT therapy.

Claim 14. for the use according to claim 13 wherein ACT therapy is selected from TCR-T, CAR-T or TILs therapies.

Claim 15. A fusion protein comprising a sequence of SEQ ID NO: 4 or a variant of SEQ ID NO: 4 having deletions and/or conservative substitutions of 1, 2, 3, 4, 5 or 6 amino acid residues.

Claim 16. A mammalian expression vector comprising a fusion protein of SEQ ID NO: 4.