

WHAT IS CLAIMED IS:

1. An IL-2 mutant comprising mutations at Y31/A73/H79; preferably, Y31V/A73L/H79Q; and more preferably further comprising mutation(s) at V91, D20 and/or H16, such as V91R, D20A or H16E compared to wild-type IL-2.

5 2. The IL-2 mutant according to claim 1, wherein the IL-2 mutant has an amino acid sequence as shown in any one of SEQ ID NO: 2, 22, 29, 32 or 37.

3. The IL-2 mutant according to any one of claim 1 to 2, wherein the IL-2 mutant has a T_m value higher than that of the wild-type IL-2.

4. The IL-2 mutant according to any one of claims 1 to 3, wherein the IL-2
10 mutant has a reduced binding ability to IL-2R $\beta\gamma$ subunit complex compared to the wild-type IL-2; preferably, the binding ability IL-2R $\beta\gamma$ subunit complex/binding ability IL-2 $\alpha\beta\gamma$ subunit complex decreases.

5. The IL-2 mutant according to any one of claim 1 to 4, wherein the mutant has a reduced stimulation ability to non-regulatory T cells or NK (natural killer) cells
15 compared to the wild-type IL-2; the stimulation can be selected from intracellular STAT5 phosphorylation or cell proliferation;

alternatively, the mutant preferentially stimulates regulatory T cells (Tregs) in peripheral blood or T cell population compared to non-regulatory T cells or NK (natural killer) cells; said preferentially stimulating can be selected from preferentially
20 stimulating STAT5 phosphorylation in regulatory T cells, preferentially stimulating regulatory T cell proliferation, increasing regulatory T cells to non-regulatory T cells ratio, or increasing regulatory T cells to NK cells ratio.

6. The IL-2 mutant according to any one of claims 1 to 5, wherein the mutation comprises deletion, insertion or substitution, preferably substitution.

7. The IL-2 mutant according to any one of claims 1 to 6, wherein the wild-type IL-2 has an amino acid sequence as shown in SEQ ID NO: 60 or SEQ ID NO: 1.

5 8. A fusion protein comprising a first polypeptide and a second polypeptide, wherein the first polypeptide is the IL-2 mutant according to any one of claims 1 to 7, and the second polypeptide is a non-IL-2 polypeptide.

9. The fusion protein according to claim 8, wherein the second polypeptide is an Fc, a tumor-antigen-binding molecule or an IL-2 receptor subunit;

10 optionally, the Fc is a human IgG Fc, for example, a human IgG1 Fc;

preferably, the human IgG1 Fc comprises at least one group of mutation(s) selected from groups (a) - (i):

(a). C220S;

(b). N297G;

15 (c). C220S and N297G;

(d). A327Q;

(e). L234A and L235A;

(f). A287C and L306C;

(g). A259C and V302C;

20 (h). R292C and V306C;

(i). V323C and I332C;

more preferably, the human IgG1 Fc has an amino acid sequence as shown in SEQ ID NO: 11;

optionally, the tumor-antigen comprises EDB-FN (extra domain of fibronectin),
 5 Muc1, p53, FAP, GD2, EpCAM, tenascin-C, CD20, CEA, MAdCAM-1 or WT1 (Wilms Tumor Protein 1); optionally, the tumor-antigen-binding molecule is an antibody, such as scFv, sdFv, Fab, Fab', F(ab')₂ or Fv;

optionally, the IL-2 receptor subunit is an IL-2 receptor α subunit.

10 10. The fusion protein according to any one of claims 8 to 9, wherein C-terminus of the first polypeptide is linked to N-terminus of the second polypeptide with or without a linker; or N-terminus of the first polypeptide is linked to C-terminus of the second polypeptide with or without a linker;

preferably, the linker is selected from: (G₄S)_n, (GGNGT)_n or (YGNGT)_n, and the n is selected from 1, 2, 3, 4 or 5;

15 15 more preferably, the C-terminus of the first polypeptide is linked to the N-terminus of the second polypeptide with a linker (G₄S)₃.

11. The fusion protein according to any one of claims 8 to 10, wherein the fusion protein comprises an amino acid sequence as shown in any one of SEQ ID NO: 13, 40, 47, 50 or 55.

20 12. A pharmaceutical composition comprising the mutant of any one of claims 1 to 7 or the fusion protein of any one of claims 8 to 11, and a pharmaceutically acceptable carrier, diluent or adjuvant;

preferably, the pharmaceutical composition is a pharmaceutical composition for injection, e.g. for intravenous or subcutaneous injection; more preferably, the pharmaceutical composition per dose comprises an effective amount of fusion protein to be administrated to a subject; most preferably, the effective amount is 0.001-10
 5 mpk, such as 0.001 mpk, 0.002 mpk, 0.003 mpk, 0.004 mpk, 0.005 mpk, 0.006 mpk, 0.007 mpk, 0.008 mpk, 0.009 mpk, 0.01 mpk, 0.02 mpk, 0.03 mpk, 0.04 mpk, 0.05 mpk, 0.06 mpk, 0.07 mpk, 0.08 mpk, 0.09 mpk, 0.1 mpk, 0.2 mpk, 0.3 mpk, 0.4 mpk, 0.5 mpk, 0.6 mpk, 0.7 mpk, 0.8 mpk, 0.9 mpk, 1 mpk, 2 mpk, 3 mpk, 4 mpk, 5 mpk, 6 mpk, 7 mpk, 8 mpk, 9 mpk or 10 mpk.

10 13. Use of the mutant of any one of claims 1 to 7 or the fusion protein of any one of claims 8 to 11 in the manufacture of a medicament for treating disease;

preferably, the medicament is a medicament for injection, e.g. for intravenous or subcutaneous injection;

preferably, the medicament per dose comprises an effective amount of fusion
 15 protein to be administrated to a subject; most preferably, the effective amount is 0.001-10 mpk, such as 0.001 mpk, 0.002 mpk, 0.003 mpk, 0.004 mpk, 0.005 mpk, 0.006 mpk, 0.007 mpk, 0.008 mpk, 0.009 mpk, 0.01 mpk, 0.02 mpk, 0.03 mpk, 0.04 mpk, 0.05 mpk, 0.06 mpk, 0.07 mpk, 0.08 mpk, 0.09 mpk, 0.1 mpk, 0.2 mpk, 0.3 mpk, 0.4 mpk, 0.5 mpk, 0.6 mpk, 0.7 mpk, 0.8 mpk, 0.9 mpk, 1 mpk, 2 mpk, 3 mpk, 4 mpk,
 20 5 mpk, 6 mpk, 7 mpk, 8 mpk, 9 mpk or 10 mpk;

preferably, the medicament is used for treating an autoimmune disease, proliferative disease, or viral infection;

more preferably, the autoimmune disease comprises rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, cutaneous lupus erythematosus, lupus nephritis, IgA nephropathy, Sjogren's syndrome, polymyositis, dermatomyositis, scleroderma, psoriasis, plaque psoriasis, alopecia areata, multiple sclerosis, amyotrophic lateral sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, graft-versus-host disease, organ transplant rejection, autoimmune hepatitis, type I diabetes, autoimmune vasculitis, eczema or asthma;

more preferably, the proliferative disease comprises neoplasm, solid tumor, hematological tumor, malignant ascites or malignant pleural effusion; wherein the solid tumor can be selected from benign or malignant, primary or metastatic, the malignant solid tumor can be selected from be a cancer or a sarcoma, for example, epithelial cell carcinoma, endothelial cell carcinoma, squamous cell carcinoma, teratoma, lung tumor, papillomavirus-induced cancer, adenocarcinoma, carcinoma, melanoma, angiosarcoma, neuroblastoma, metastatic lung cancer, non-small cell lung cancer, small cell lung cancer, breast cancer, Merkel cell cancer, ovarian cancer, renal cell cancer, metastatic renal cancer, head and neck cancer, bladder cancer, non-muscle invasive bladder cancer; hematological tumor can be selected from leukemia, lymphoma, multiple myeloma, such as B-cell lymphoma, T-cell lymphoma, cutaneous T-cell lymphoma, T-cell large granular lymphocytic leukemia;

more preferably, the viral infection is selected from HIV infection, novel coronavirus infection or HPV viral infection.