

Claims

1. An immunocompetent cell that expresses: (a) a chimeric antigen receptor (CAR) specifically recognizing human mesothelin; (b) an exogenous interleukin 7 (IL-7); and (c) an exogenous chemokine (C-C motif) ligand 19 (CCL19),

wherein the CAR comprising a single chain antibody, a transmembrane region, and a signaling region that induces activation of the immunocompetent cell,

and wherein the single chain antibody in the CAR is (1-1) a single chain antibody comprising a heavy chain variable region comprising heavy chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 13, heavy chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 14, and heavy chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 15; and a light chain variable region comprising light chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 16, light chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 17, and light chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 18.

2. The immunocompetent cell according to claim 1, wherein the immunocompetent cell is an immunocompetent cell separated from a living body.

3. The immunocompetent cell according to claim 1 or 2, wherein the immunocompetent cell comprises an exogenous nucleic acid encoding the CAR specifically recognizing human mesothelin, an exogenous nucleic acid encoding IL-7, and an exogenous nucleic acid encoding CCL19.

4. The immunocompetent cell according to claim 3, wherein the exogenous nucleic acid encoding IL-7, and the exogenous nucleic acid encoding CCL19 are an exogenous nucleic acid encoding human IL-7, and an exogenous nucleic acid encoding human CCL19.

5. The immunocompetent cell according to claim 4, wherein the exogenous nucleic acid encoding the CAR specifically recognizing human mesothelin, the exogenous nucleic acid encoding human IL-7, and the exogenous nucleic acid encoding human CCL19 are integrated into the genome.

6. The immunocompetent cell according to any one of claims 1 to 5, wherein the single chain antibody in the CAR is a single chain antibody comprising a heavy chain variable region consisting of an amino acid sequence having 85% or higher sequence identity to the amino acid sequence shown by SEQ ID NO:1, and comprising heavy chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 13, heavy

chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 14, and heavy chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 15; and a light chain variable region consisting of an amino acid sequence having 85% or higher sequence identity to the amino acid sequence shown by SEQ ID NO: 2, and comprising light chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 16, light chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 17, and light chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 18.

7. The immunocompetent cell according to any one of claims 1 to 6, wherein the single chain antibody in the CAR is:

a single chain antibody comprising a heavy chain variable region consisting of the amino acid sequence shown by SEQ ID NO: 1, and a light chain variable region consisting of the amino acid sequence shown by SEQ ID NO: 2.

8. The immunocompetent cell according to any one of claims 1 to 7, wherein the transmembrane region in the CAR comprises an amino acid sequence having 85% or higher sequence identity to the amino acid sequence shown by SEQ ID NO: 7.

9. The immunocompetent cell according to any one of claims 1 to 8, wherein the signaling region that induces activation of the immunocompetent cell in the CAR comprises:

(i) a polypeptide that comprises an amino acid sequence having 85% or higher sequence identity to the amino acid sequence shown by SEQ ID NO: 9, or a polypeptide that consists of an amino acid sequence derived from the amino acid sequence shown by SEQ ID NO: 9 by the deletion, substitution, insertion, and/or addition of one or several amino acids; and

(ii) a polypeptide that comprises an amino acid sequence having 85% or higher sequence identity to the amino acid sequence shown by SEQ ID NO: 10, or a polypeptide that consists of an amino acid sequence derived from the amino acid sequence shown by SEQ ID NO: 10 by the deletion, substitution, insertion, and/or addition of one or several amino acids.

10. The immunocompetent cell according to claim 9, wherein the signaling region that induces activation of the immunocompetent cell in the CAR further comprises the amino acid sequence shown by SEQ ID NO: 8.

11. The immunocompetent cell according to any one of claims 1 to 10, wherein the heavy chain variable region and the light chain variable region are connected via a peptide linker consisting of a 2- to 30-amino

acid sequence.

12. The immunocompetent cell according to claim 11, wherein the peptide linker consists of the amino acid sequence shown by SEQ ID NO: 26 or SEQ ID NO: 27.

13. The immunocompetent cell according to any one of claims 1 to 12, wherein the light chain variable region is positioned on a C-terminal side of the heavy chain variable region.

14. The immunocompetent cell according to any one of claims 1 to 13, wherein the single chain antibody in the CAR is:

a single chain antibody sequentially comprising a heavy chain variable region consisting of the amino acid sequence shown by SEQ ID NO: 1, a peptide linker consisting of the amino acid sequence shown by SEQ ID NO: 26, and a light chain variable region consisting of the amino acid sequence shown by SEQ ID NO: 2.

15. The immunocompetent cell according to any one of claims 1 to 14, wherein the immunocompetent cell is a T cell.

16. The immunocompetent cell according to any one of claims 1 to 15, wherein the immunocompetent cell is a T cell derived from a human or separated from a human.

17. A pharmaceutical composition comprising the immunocompetent cell according to any one of claims 1 to 16 and a pharmaceutically acceptable additive.

18. The pharmaceutical composition according to claim 17 for use in the treatment of a cancer type highly expressing mesothelin in a cancer tissue, or a cancer type derived from cancer cells highly expressing mesothelin,
wherein the immunocompetent cell is a T cell or an NK cell.

19. An expression vector comprising a nucleic acid encoding a chimeric antigen receptor (CAR) specifically recognizing human mesothelin, a nucleic acid encoding IL-7, and a nucleic acid encoding CCL19, the CAR comprising a single chain antibody, a transmembrane region, and a signaling region that induces activation of an immunocompetent cell, wherein the single chain antibody in the CAR is a single chain antibody comprising a heavy chain variable region comprising heavy chain CDR1 consisting of the amino acid

sequence shown by SEQ ID NO: 13, heavy chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 14, and heavy chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 15; and a light chain variable region comprising light chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 16, light chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 17, and light chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 18.

20. A method for producing an immunocompetent cell that expresses a chimeric antigen receptor (CAR) specifically recognizing human mesothelin, IL-7, and CCL19, comprising introducing a nucleic acid encoding the CAR specifically recognizing human mesothelin, a nucleic acid encoding the IL-7, and a nucleic acid encoding the CCL19 to an immunocompetent cell, the CAR comprising a single chain antibody, a transmembrane region, and a signaling region that induces activation of the immunocompetent cell, wherein the single chain antibody in the CAR is a single chain antibody comprising a heavy chain variable region comprising heavy chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 13, heavy chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 14, and heavy chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 15; and a light chain variable region comprising light chain CDR1 consisting of the amino acid sequence shown by SEQ ID NO: 16, light chain CDR2 consisting of the amino acid sequence shown by SEQ ID NO: 17, and light chain CDR3 consisting of the amino acid sequence shown by SEQ ID NO: 18.