【Claims】

1. An artificially engineered immune cell having at least one artificially engineered immune regulatory genes selected from Dgkα gene and Dgkζ gene,

wherein the artificially engineered immune regulatory gene includes one or more indels,

wherein, based on a wild-type nucleotide sequence of the immune regulatory gene, the indels are located in a proto-spacer-adjacent Motif (PAM) sequence or the indels are located within the range of continuous 1bp to 30bp adjacent to the 5' end or the 3' end of a PAM sequence, and the indels are located in a sequence selected from SEQ ID NOs: 19, 20, 21 and 23 in an exon region of Dgkα gene, and SEQ ID NOs: 109 to 113 in an exon region of Dgkζ gene,

wherein the engineered Dgkα gene does not comprise the same nucleotide sequence selected from SEQ ID NOs: 19, 20, 21 and 23 on an exon region of the engineered Dgkα gene, and

wherein the engineered Dgkζ gene does not comprises the same nucleotide sequence selected from SEQ ID NOs: 109 to 113 on an exon region of the engineered Dgkζ gene.

2. The artificially engineered immune cell according to claim 1, wherein the indels are located in a sequence selected from SEQ ID NOs: 19, 20, 21 and 23 in an exon of Dgkα gene, and a sequence from selected from SEQ ID NOs: 109 to 113 in an exon region of Dgkζ gene.

3. The artificially engineered immune cell according to claim 1 or claim 2, wherein the engineered Dgkα gene does not comprise the same nucleotide sequence as SEQ ID NO: 19 on exon 7 of the Dgkα gene, or the engineered Dgkα gene does not comprise the same nucleotide sequence as at least one selected from SEQ ID NOs: 20, 21, and 23 on exon 8 of the Dgkα gene.

4. The artificially engineered immune cell according to any one of claims 1 to 3, wherein the engineered Dgkζ gene does not comprise the same nucleotide sequence as at least one selected from SEQ ID NOs: 109 to 113 on exon 3 of the Dgkζ gene.

5. The artificially engineered immune cell according to any one of claims 1 to 4, wherein the immune cell is at least one cell selected from the group consisting of T cell, NK cell NKT cell, and an immune cell differentiated from a stem cell.

6. The artificially engineered immune cell according to any one of claims 1 to 5, wherein the immune cell further comprises a chimeric antigen receptor or an engineered T cell receptor.

7. A composition for producing of an artificially engineered immune cell having at least one artificially engineered immune regulatory genes selected from Dgkα gene and Dgkζ gene, comprising:

(i) at least one guide nucleic acid capable of targeting a target sequence located in an exon region of Dgkα gene or Dgkζ gene, or nucleic acid encoding the guide nucleic acid; and

(ii) an editor protein or a nucleic acid encoding the editor protein, wherein the guide nucleic acid and the editor protein are capable of forming a guide nucleic acid-editor protein complex, and the guide nucleic acid-editor protein complex is capable of manipulating the target sequence;

wherein the guide nucleic acid comprises:

a guide domain, a first complementary domain, a linker domain, and a second complementary domain, wherein the guide domain consists of the 1st to the 20th base of a nucleotide sequence selected from SEQ ID NOs: 19, 20, 21, 23, 109, 110, 111, 112 and 113, in which the guide domain contains U instead of T present in the 1st to 20th base of the selected nucleotide sequence as an RNA sequence and the guide domain has 0 to 5 mismatches to the 1st to 20th base of the selected nucleotide sequence, and

wherein the editor protein is a Cas9 protein.

8. The composition according to claim 7, wherein the guide nucleic acids and the editor protein are in the form of ribonucleoprotein.

9. The composition according to claim 7,

wherein the composition comprises two or more guide nucleic acids which comprises a guide nucleic acid for targeting Dgkα gene and a guide nucleic acid for targeting Dgkζ gene,

wherein the guide nucleic acid for targeting Dgkα gene comprises the guide domain consisting of the 1st to the 20th base of a nucleotide sequence selected from SEQ ID NOs: 19, 20, 21 and 23, and the guide nucleic acid for targeting Dgkζ gene comprises the guide domain consisting of the 1st to the 20th base of a nucleotide sequence selected from SEQ ID NOs: 109, 110, 111, 112 and 113, in which the guide domain contains U instead of T present in the 1st to 20th base of the selected nucleotide sequence as an RNA sequence.

10. A guide nucleic acid for targeting a target sequence located in an exon region of Dgkα gene or Dgkζ gene, comprising a guide domain, a first complementary domain, a linker domain, and a second complementary domain,

wherein the guide domain consists of the 1st to the 20th base of a nucleotide sequence selected from SEQ ID NOs: 19, 20, 21, 23, 109, 110, 111, 112 and 113, in which the guide domain contains U instead of T present in the 1st to 20th base of the selected nucleotide sequence as an RNA sequence and the guide domain has 0 to 5 mismatches to the 1st to 20th base of the selected nucleotide sequence.

11. A method for producing an artificially engineered immune cell having at least one artificially engineered immune regulatory genes selected from Dgkα gene and Dgkζ gene, comprising:

contacting an immune cell isolated from a mammal to:

(i) at least one guide nucleic acid capable of targeting a target sequence located in an exon region of Dgkα gene or Dgkζ gene, or nucleic acid encoding the guide nucleic acid, and

(ii) an editor protein which is a Streptococcus pyogenes-derived Cas9 protein or a Campylobacter jejuni-derived Cas9 protein, or a nucleic acid encoding the editor protein, where the guide nucleic acid and the editor protein are capable of forming a guide nucleic

acid-editor protein complex, and the guide nucleic acid-editor protein complex is capable of manipulating the target sequence,

wherein the guide nucleic acid comprises a guide domain, a first complementary domain, a linker domain, and a second complementary domain, wherein the guide domain consists of the 1st to the 20th base of a nucleotide sequence selected from SEQ ID NOs: 19, 20, 21, 23, 109, 110, 111, 112 and 113, in which the guide domain contains U instead of T present in the 1st to 20th base of the selected nucleotide sequence as an RNA sequence and the guide domain has 0 to 5 mismatches to the 1st to 20th base of the selected nucleotide sequence; and

inducing at least one indel in the nucleic acid sequence of Dgkα gene or Dgkζ gene of the immune cell,

wherein, based on a wild-type nucleotide sequence of the immune regulatory gene, the indels are located in a proto-spacer-adjacent Motif (PAM) sequence or the indels are located within the range of 1bp to 30bp adjacent to the 5' end or the 3' end of a PAM sequence,

whereby the artificially engineered immune cell has the engineered Dgkα gene which does not comprise the same nucleotide sequence selected from SEQ ID NOs: 19, 20, 21 and 23 on an exon region of the engineered Dgkα gene and/or the artificially engineered immune cell has the engineered Dgkζ gene which does not comprise the same nucleotide sequence selected from SEQ ID NOs: 109 to 113 on an exon region of the engineered Dgkζ gene.

12. The method according to claim 11, wherein the step of contacting is carried out by one or more methods selected from electroporation, liposome, plasmid, viral vectors, nanoparticle and protein translocation domain fusion protein method.

13. The method according to claim 12, wherein the viral vector is at least one selected from the group of a retrovirus, a lentivirus, an adenovirus, an adeno-associated virus, a vaccinia virus, a poxvirus, and a herpes simplex virus.

14. The method according to any one of claims 11 to 13, wherein the immune cell isolated from a mammal is an immune cell isolated from the human body.

15. The method according to any one of claims 11 to 14, wherein the immune cell isolated from a mammal is at least one cell selected from the group consisting of T cell, NK cell, NKT cell, and an immune cell differentiated from a stem cell.