

CLAIMS

1. A cell in which at least one HLA allele is disrupted or modified and at least one kind of HLA protein can be expressed.
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2. The cell according to claim 1, wherein the HLA allele includes an HLA-A allele, an HLA-B allele, or an HLA-C allele.
3. The cell according to claim 2, wherein at least one kind of HLA allele of the HLA-A
10 allele, the HLA-B allele, or the HLA-C allele is homozygous.
4. The cell according to any one of claims 1 to 3, which is a low-antigenic cell in which a rejection reaction is reduced in a case where the cell is allogeneically transplanted into a recipient, and in which the disrupted or modified HLA allele is an HLA allele that is not
15 present in the recipient.
5. The cell according to any one of claims 1 to 4, which is a pluripotent stem cell.
6. The cell according to any one of claims 1 to 5, wherein at least one allele of a class II
20 major histocompatibility complex transactivator (CIITA) allele, a regulatory factor X5 (RFX5) allele, a regulatory factor X associated protein (RFXAP) allele, or a regulatory factor X associated ankyrin containing protein (RFXANK) allele is further disrupted or modified.
- 25 7. The cell according to any one of claims 1 to 6, in which the HLA-A allele and the

HLA-B allele are disrupted and at least one kind of HLA-C protein can be expressed.

8. The cell according to claim 7, wherein the HLA-C protein is a protein encoded by one kind of allele selected from the group consisting of an HLA-C*01:02 allele, an HLA-C*02:02 allele, an HLA-C*03:03 allele, an HLA-C*03:04 allele, an HLA-C*04:01 allele, an HLA-C*05:01 allele, an HLA-C*06:02 allele, an HLA-C*07:01 allele, an HLA-C*07:02 allele, an HLA-C*08:01 allele, an HLA-C*12:02 allele, and an HLA-C*16:01 allele.

9. A method for producing the cell according to any one of claims 1 to 8, comprising a step of disrupting or modifying an HLA allele of a donor cell by genome editing.

10. The method for producing according to claim 9, wherein the genome editing is performed by introducing a sequence-specific DNA-cleaving enzyme into the donor cell.

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11. The method for producing according to claim 10, wherein the sequence-specific DNA-cleaving enzyme is CRISPR-Cas and the genome editing is performed by introducing a gRNA and the CRISPR-Cas into the donor cell.

12. The method for producing according to any one of claims 9 to 11, wherein the donor cell is a pluripotent stem cell.

13. A gRNA targeting, as a target base sequence, a base sequence that is mapped to only one target HLA haplotype in a case where the base sequence is mapped to base sequence data of genomic DNA of all HLA haplotypes, but that is not mapped in a case

where the base sequence is mapped to base sequence data of all genomic DNA except for HLA alleles.

14. The gRNA according to claim 13,

5 wherein the target base sequence consists of

a base sequence set forth in any of SEQ ID NOs: 3, 4, 7, 45 to 52, and
72 to 2459, or

a base sequence in which one or several bases are deleted, substituted,
or added at a 5' end of a base sequence set forth in any of SEQ ID NOs: 3, 4, 7, 45 to 52,

10 and 72 to 2459.

15. The gRNA according to claim 13 or 14,

wherein the target base sequence consists of

a base sequence set forth in any of SEQ ID NOs: 3, 4, 7, and 45 to 52,
15 or

a base sequence in which one or several bases are deleted, substituted,
or added at a 5' end of a base sequence set forth in any of SEQ ID NOs: 3, 4, 7, and 45 to
52.

20 16. The gRNA according to any one of claims 13 to 15, wherein the target base
sequence is mapped to an exon 2 or 3 of an HLA gene.

17. A gRNA targeting, as a target base sequence, a base sequence that is mapped to two
or more target HLA haplotypes in a case where the base sequence is mapped to base

25 sequence data of genomic DNA of all HLA haplotypes, but that is not mapped in a case

where the base sequence is mapped to base sequence data of all genomic DNA except for HLA alleles.

18. The gRNA according to claim 17,

5 wherein the target base sequence consists of

a base sequence set forth in any of SEQ ID NOs: 53 to 55 and 2460 to 8013, or

a base sequence in which one or several bases are deleted, substituted, or added at a 5' end of a base sequence set forth in any of SEQ ID NOs: 53 to 55 and

10 2460 to 8013.

19. The gRNA according to claim 17 or 18,

wherein the target base sequence consists of

a base sequence set forth in any of SEQ ID NOs: 53 to 55, or

15 a base sequence in which one or several bases are deleted, substituted, or added at a 5' end of a base sequence set forth in any of SEQ ID NOs: 53 to 55.

20. The gRNA according to any one of claims 17 to 19, wherein the target base sequence is mapped to an exon 2 or 3 of an HLA gene.

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21. The method for producing according to claim 11, wherein the gRNA is the gRNA according to any one of claims 13 to 20.

22. A method for specifying a target base sequence for producing, by genome editing, a
25 low-antigenic cell in which a rejection reaction is reduced in a case where the cell is

allogeneically transplanted into a recipient, the method comprising:

mapping a candidate base sequence to base sequence data of genomic DNA of all HLA haplotypes;

mapping the candidate base sequence to base sequence data of all genomic DNA except for HLA alleles; and

specifying, as a target base sequence, the candidate base sequence that is mapped to only one target HLA haplotype in a case where the base sequence is mapped to base sequence data of genomic DNA of all HLA haplotypes, but that is not mapped in a case where the base sequence is mapped to base sequence data of all genomic DNA except for the HLA alleles.

23. A method for specifying a target base sequence for producing, by genome editing, a low-antigenic cell in which a rejection reaction is reduced in a case where the cell is allogeneically transplanted into a recipient, the method comprising:

mapping a candidate base sequence to base sequence data of genomic DNA of all HLA haplotypes;

mapping the candidate base sequence to base sequence data of all genomic DNA except for HLA alleles; and

specifying, as a target base sequence, the candidate base sequence that is mapped to two or more target HLA haplotypes in a case where the base sequence is mapped to base sequence data of genomic DNA of all HLA haplotypes, but that is not mapped in a case where the base sequence is mapped to base sequence data of all genomic DNA except for the HLA alleles.