

## CLAIMS

1. An anti-PAD4 antibody or an antibody fragment thereof, wherein heavy chain complementarity determining region (HCDR)~~1~~ comprises an amino acid sequence of SEQ ID NO: 1, HCDR2 comprises an amino acid sequence of SEQ ID NO: 2, HCDR3 comprises an amino acid sequence of SEQ ID NO: 3, light chain complementarity determining region (LCDR)~~1~~~~LCDR1~~ comprises an amino acid sequence of SEQ ID NO: 4, LCDR2 comprises an amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises an amino acid sequence of SEQ ID NO: 6.
2. The anti-PAD4 antibody or the antibody fragment thereof according to claim 1, wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, HCDR2 comprises any one of amino acid sequences of SEQ ID NOs: 7 – 10, HCDR3 comprises an amino acid sequence of SEQ ID NO: 11 or 12, LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises any one of amino acid sequences of SEQ ID NOs: 13 – 15.
3. The anti-PAD4 antibody or the antibody fragment thereof according to claim 1 or 2, wherein said anti-PAD4 antibody or the antibody fragment thereof is selected from the group consisting of:
  - (a-1) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, HCDR2 comprises the amino acid sequence of SEQ ID NO: 7, HCDR3 comprises the amino acid sequence of SEQ ID NO: 11, LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 13;
  - (b-1) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, HCDR2 comprises the amino acid sequence of SEQ ID NO: 8, HCDR3 comprises the amino acid sequence of SEQ ID NO: 11,

LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 13;

(c-1) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, HCDR2 comprises the amino acid sequence of SEQ ID NO: 9, HCDR3 comprises the amino acid sequence of SEQ ID NO: 12, LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 14; and

(d-1) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, HCDR2 comprises the amino acid sequence of SEQ ID NO: 10, HCDR3 comprises the amino acid sequence of SEQ ID NO: 11, LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 15.

4. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 3, wherein said anti-PAD4 antibody or the antibody fragment thereof is selected from the group consisting of:

(a-2) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 consists of the amino acid sequence of SEQ ID NO: 1, HCDR2 consists of the amino acid sequence of SEQ ID NO: 7, HCDR3 consists of the amino acid sequence of SEQ ID NO: 11, LCDR1 consists of the amino acid sequence of SEQ ID NO: 4, LCDR2 consists of the amino acid sequence of SEQ ID NO: 5, and LCDR3 consists of the amino acid sequence of SEQ ID NO: 13;

(b-2) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 consists of the amino acid sequence of SEQ ID NO: 1, HCDR2 consists of the amino acid sequence of SEQ ID NO: 8, HCDR3 consists of the amino acid sequence of SEQ ID NO: 11, LCDR1 consists of the amino acid sequence of SEQ ID NO: 4, LCDR2 consists of the amino acid sequence of SEQ ID NO: 5, and LCDR3 consists of the amino acid sequence of SEQ ID NO: 13;

(c-2) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 consists of the amino acid sequence of SEQ ID NO: 1, HCDR2 consists of the amino acid sequence of SEQ ID NO: 9, HCDR3 consists of the amino acid sequence of SEQ ID NO: 12, LCDR1

consists of the amino acid sequence of SEQ ID NO: 4, LCDR2 consists of the amino acid sequence of SEQ ID NO: 5, and LCDR3 consists of the amino acid sequence of SEQ ID NO: 14; and

(d-2) an anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 consists of the amino acid sequence of SEQ ID NO: 1, HCDR2 consists of the amino acid sequence of SEQ ID NO: 10, HCDR3 consists of the amino acid sequence of SEQ ID NO: 11, LCDR1 consists of the amino acid sequence of SEQ ID NO: 4, LCDR2 consists of the amino acid sequence of SEQ ID NO: 5, and LCDR3 consists of the amino acid sequence of SEQ ID NO: 15.

5. An anti-PAD4 antibody or an antibody fragment thereof, wherein said anti-PAD4 antibody or the antibody fragment thereof is selected from the group consisting of:

(a-3) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region comprises an amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 16, and a light chain variable region comprises an amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 17;

(b-3) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region comprises an amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 18, and a light chain variable region comprises an amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 19;

(c-3) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region comprises an amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 20, and a light chain variable region comprises an amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 21; and

(d-3) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region comprises an amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 22, and a light chain variable region comprises an amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 23.

6. The anti-PAD4 antibody or the antibody fragment thereof according to claim 5, wherein said anti-PAD4 antibody or the antibody fragment thereof is selected from the group consisting of:

(a-4) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region consists of the amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 16, and a light chain variable region consists of the amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 17;

(b-4) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region consists of the amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 18, and a light chain variable region consists of the amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 19;

(c-4) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region consists of the amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 20, and a light chain variable region consists of the amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 21; and

(d-4) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region consists of the amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 22, and a light chain variable region consists of the amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 23.

7. The anti-PAD4 antibody or the antibody fragment thereof according to claim 5 or 6, wherein said anti-PAD4 antibody or the antibody fragment thereof is selected from the group consisting of:

(a-5) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain consists of an amino acid sequence of SEQ ID NO: 16, and a light chain consists of an amino acid sequence of SEQ ID NO: 17;

(b-5) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain consists of an amino acid sequence of SEQ ID NO: 18, and a light chain consists of an amino acid sequence of SEQ ID NO: 19;

(c-5) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain consists of an amino acid sequence of SEQ ID NO: 20, and a light chain consists of an amino acid sequence of SEQ ID NO: 21; and

(d-5) an anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain consists of an amino acid sequence of SEQ ID NO: 22, and a light chain consists of an amino acid sequence of SEQ ID NO: 23.

8. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 7, wherein an amino acid corresponding to the 84th amino acid of a heavy chain is serine.

9. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 8, wherein a KD value with respect to PAD4 is 100 pM or less.

10. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 9, wherein said anti-PAD4 antibody or the antibody fragment thereof has a binding amount of 90% or more when the anti-PAD4 antibody or the antibody fragment thereof is stored at 40 °C for one month as compared to a PAD4-binding amount of the anti-PAD4 antibody or the antibody fragment thereof before the storage.

11. e-1) An anti-PAD4 antibody or an antibody fragment thereof, wherein HCDR1 comprises an amino acid sequence of SEQ ID NO: 1, HCDR2 comprises an amino acid sequence of SEQ ID NO: 24, HCDR3 comprises an amino acid sequence of SEQ ID NO: 11, LCDR1 comprises an amino acid sequence of SEQ ID NO: 4, LCDR2 comprises an amino acid sequence of SEQ ID NO: 5, and LCDR3 comprises an amino acid sequence of SEQ ID NO: 25, wherein an amino acid corresponding to the 84th amino acid of a heavy chain is serine.

12. e-2) The anti-PAD4 antibody or the antibody fragment thereof according to claim 11, wherein HCDR1 consists of the amino acid sequence of SEQ ID NO: 1, HCDR2 consists of the

amino acid sequence of SEQ ID NO: 24, HCDR3 consists of the amino acid sequence of SEQ ID NO: 11, LCDR1 consists of the amino acid sequence of SEQ ID NO: 4, LCDR2 consists of the amino acid sequence of SEQ ID NO: 5, and LCDR3 consists of the amino acid sequence of SEQ ID NO: 25, wherein the amino acid corresponding to the 84th amino acid of a heavy chain is serine.

13. e-4) An anti-PAD4 antibody or an antibody fragment thereof, wherein a heavy chain variable region comprises an amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 28, and a light chain variable region comprises an amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 27.

14. e-5) The anti-PAD4 antibody or the antibody fragment thereof according to claim 13, wherein a heavy chain variable region consists of the amino acid sequence of amino acid numbers 1 – 120 of SEQ ID NO: 28, and a light chain variable region consists of the amino acid sequence of amino acid numbers 1 – 105 of SEQ ID NO: 27.

15. The anti-PAD4 antibody or the antibody fragment thereof according to claim 13 or 14, wherein a heavy chain consists of SEQ ID NO: 28 and a light chain consists of SEQ ID NO: 27.

16. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 11 – 15, wherein cleavage occurring during generation is less than 3% of a total generation amount.

17. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 16, wherein the antibody is a neutralizing antibody.

18. The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 17, wherein the antibody is a PAD4 binding antibody represented by SEQ ID NO: 29.

19. A nucleic acid molecule comprising a base sequence encoding the anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – ~~18~~15.
20. A recombinant vector comprising the nucleic acid molecule according claim 19.
21. A transformant comprising the recombinant vector according to claim 20.
22. A pharmaceutical composition comprising the anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 18.
23. The pharmaceutical composition according to claim 22, wherein said pharmaceutical composition is a preventive agent or a therapeutic agent for rheumatoid arthritis or arthritis, systemic lupus erythematosus, lupus nephritis, or graft-versus-host disease.
24. The pharmaceutical composition according to claim 22 or 23, wherein said pharmaceutical composition is an inhibiting agent of citrullination in a protein.
25. The pharmaceutical composition according to any one of claims 22 – 24, wherein said pharmaceutical composition is an inhibiting agent of netosis in cells.
26. ~~Use of the~~The anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 18 or the pharmaceutical composition according to any one of claims 22 – 25 for ~~preventing or treating rheumatoid arthritis or arthritis, systemic lupus erythematosus, lupus nephritis, or graft versus host disease~~use as a medicament.

27. Use of the anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1 – 18 or the pharmaceutical composition according to any one of claims 22 – 25 in the manufacture of a ~~preventive agent or a therapeutic agent~~medicament for preventing or treating rheumatoid arthritis or arthritis, systemic lupus erythematosus, lupus nephritis, or graft-versus-host disease.

28. ~~A method~~The use of claim 27 for preventing or treating rheumatoid arthritis or arthritis, systemic lupus erythematosus, lupus nephritis, or graft-versus-host disease, wherein the ~~said method comprising administering an effective amount of the anti-PAD4 antibody or the antibody fragment thereof according to any one of claims 1—18 or the pharmaceutical composition according to any one of claims 22—25 to a subject in need thereof.~~