

CLAIMS

1. An antibody which binds to kallikrein 5 (KLK5), wherein the antibody comprises a variable light chain and a variable heavy chain, and wherein:
 - a. the variable light chain comprises a CDR-L1 comprising SEQ ID NO: 1 or SEQ ID NO: 62 or SEQ ID NO: 63, a CDR-L2 comprising SEQ ID NO: 2 and a CDR-L3 comprising SEQ ID NO: 3; and
 - b. the variable heavy chain comprises a CDR-H1 comprising SEQ ID NO: 4, a CDR-H2 comprising SEQ ID NO: 5 and a CDR-H3 comprising SEQ ID NO: 6.
2. An antibody which binds to kallikrein 5 (KLK5), wherein the antibody binds to an epitope of human KLK5 comprising amino acid residues Arg87, Ala107, Arg110, Lys111, Lys112, Val113, Val137, Lys138, Ser139, Ile140, Pro141, His142, Pro143, Tyr145, Ser146 and His147 with reference to SEQ ID NO: 51; wherein, the antibody comprises a variable light chain and a variable heavy chain, and wherein:
 - a. the variable light chain comprises a CDR-L1 comprising SEQ ID NO: 1 or SEQ ID NO: 62 or SEQ ID NO: 63, preferably a CDR-L1 comprising SEQ ID NO: 1, a CDR-L2 comprising SEQ ID NO: 2 and a CDR-L3 comprising SEQ ID NO: 3; and
 - b. the variable heavy chain comprises a CDR-H1 comprising SEQ ID NO: 4, a CDR-H2 comprising SEQ ID NO: 5 and a CDR-H3 comprising SEQ ID NO: 6; and wherein optionally the epitope is characterized by X-ray crystallography.
3. The antibody according to any one of claims 1 to 2, wherein
 - A) the antibody inhibits or reduces the protease activity of KLK5; and/or
 - B) wherein the antibody binds to KLK5 when KLK5 is bound to LEKTI, or a fragment of LEKTI; and/or
 - C) wherein the antibody does not compete with LEKTI, or a fragment of LEKTI, for binding KLK5; and/or
 - D) wherein the antibody forms a complex with KLK5 bound to LEKTI, or a fragment of LEKTI.

4. The antibody according to claim 3 wherein the fragment of LEKTI is human LEKTI domain 5 comprising amino acids 1 to 64 of SEQ ID NO: 54 or LEKTI domain 8 comprising amino acids 1 to 71 of SEQ ID NO: 61; and/or

wherein the antibody binds human KLK5, preferably human KLK5 comprising SEQ ID NO: 53 and cynomolgus monkey (cyno) KLK5, preferably cyno KLK5 comprising SEQ ID NO: 60; and/or

wherein the antibody does not bind human or cyno kallikrein 2 (KLK2); or human or cyno kallikrein 4 (KLK4); or human or cyno kallikrein 7 (KLK7).
5. The antibody according to any one of the preceding claims wherein the antibody is a chimeric or humanized antibody.
6. The antibody according to any one of the preceding claims, wherein the antibody is a full-length antibody; wherein, optionally, the full-length antibody is selected from an IgG1, IgG4 or IgG4P.
7. The antibody according to any one of claims 1 to 6, wherein the antibody comprises:
 - a. a variable light chain comprising SEQ ID NO: 7 or 11 or 15 or 19 or 23; and/or
 - b. a variable heavy chain comprising SEQ ID NO: 9 or 27 or 31 or 35 or 39 or 43; and/or
 - c. a light chain comprising SEQ ID NO: 13 or 17 or 21 or 25; and
 - d. a heavy chain comprising SEQ ID NO: 29 or 33 or 37 or 41 or 45.
8. The antibody according to claim 7, wherein amino acid residue glutamine (Gln; Q) in L-CDR1 at position 24 with reference to SEQ ID NO: 15 or 17 is replaced by arginine (Arg; R) or by lysine (Lys; K).
9. The antibody according to any one of the preceding claims wherein KLK5 is human KLK5 comprising SEQ ID NO: 51 or 52 or 53 or cyno KLK5 comprising SEQ ID NO: 60.
10. An isolated polynucleotide encoding the antibody according to any one of claims 1 to 9; wherein preferably, the polynucleotide encodes:
 - a. a light chain variable region, wherein the polynucleotide:

i. is at least 90% identical to SEQ ID NO: 8 (or nucleotides 1 to 330 of SEQ ID NO: 8) or 12 (or nucleotides 1 to 330 of SEQ ID NO: 12) or 16 or 20 or 24 or 64 or 66; or

ii. comprises SEQ ID NO: 8 (or nucleotides 1 to 330 of SEQ ID NO: 8) or 12 (or nucleotides 1 to 330 of SEQ ID NO: 12) or 16 or 20 or 24 or 64 or 66; or

iii. consists essentially of SEQ ID NO: 8 (or nucleotides 1 to 330 of SEQ ID NO: 8) or 12 (or nucleotides 1 to 330 of SEQ ID NO: 12) or 16 or 20 or 24 or 64 or 66; or

b. a heavy chain variable region, wherein the polynucleotide:

i. is at least 90% identical to SEQ ID NO: 10 or 28 or 32 or 36 or 40 or 44; or

ii. comprises SEQ ID NO: 10 or 28 or 32 or 36 or 40 or 44; or

iii. consists essentially of SEQ ID NO: 10 or 28 or 32 or 36 or 40 or 44; or

c. a light chain, wherein the polynucleotide:

i. is at least 90% identical to SEQ ID NO: 14 or 18 or 22 or 26 or 65 or 67 or 100 or 101 or 102 or 103 or 104; or

ii. comprises SEQ ID NO: 14 or 18 or 22 or 26 or 65 or 67 or 100 or 101 or 102 or 103 or 104; or

iii. consists essentially of SEQ ID NO: 14 or 18 or 22 or 26 or 65 or 67 or 100 or 101 or 102 or 103 or 104; or

d. a heavy chain, wherein the polynucleotide:

i. is at least 90% identical to SEQ ID NO: 30 or 34 or 38 or 42 or 46; or

ii. comprises SEQ ID NO: 30 or 34 or 38 or 42 or 46; or

iii. consists essentially of SEQ ID NO: 30 or 34 or 38 or 42 or 46.

11. A cloning or expression vector comprising one or more polynucleotides according to claim 10.

12. A host cell comprising:
 - a. one or more polynucleotides according to claim 10 or
 - b. one or more expression vectors according to claim 11.
13. A process for the production of an antibody according to any one of claims 1 to 9, comprising culturing the host cell according to claim 12 under suitable conditions for producing the antibody and isolating the antibody produced by the host cell.
14. A pharmaceutical composition comprising the antibody according to any one of claims 1 to 9 and one or more pharmaceutically acceptable carriers, excipients or diluents.
15. The antibody according to any one of claims 1 to 9 or the pharmaceutical composition according to claim 14 for use in the treatment of a disease characterized by dysregulation of KLK5 or by dysregulation of inhibition of KLK5; wherein the disease is preferably selected from Netherton's Syndrome, Atopic Dermatitis, Ichthyoses, Rosacea, Asthma or Cancer, such as ovarian cancer or bladder cancer or a combination thereof; more preferably, Atopic Dermatitis.