

Claims

1. An isolated, synthetic or recombinant antibody, or functional part or functional equivalent thereof, that is specific for an epitope of CD9 comprising at least one amino acid selected from the group consisting of K169, D171, V172 and L173 of the CD9 sequence as depicted in Figure 2.
2. An isolated, synthetic or recombinant antibody or functional part or functional equivalent according to claim 1, that is specific for an epitope of CD9 comprising amino acids corresponding to K169, D171, V172, L173 and F176 of the CD9 sequence as depicted in Figure 2.
3. An isolated, synthetic or recombinant antibody or a functional part or a functional equivalent according to claim 1 or 2, that comprises:
 - a heavy chain CDR1 sequence that has at least 80% sequence identity with the sequence DYAMH; and
 - a heavy chain CDR2 sequence that has at least 80% sequence identity with the sequence GISWNSGSIVYADSVKG; and
 - a heavy chain CDR3 sequence that has at least 80% sequence identity with the sequence AVSGYYPYFDY; and
 - a light chain CDR1 sequence that has at least 80% sequence identity with the sequence KSSQSVLYSSNNKNYLG; and
 - a light chain CDR2 sequence that has at least 80% sequence identity with the sequence WASTRES; and
 - a light chain CDR3 sequence that has at least 80% sequence identity with the sequence QYYTTP.
4. An antibody or functional part or functional equivalent according to any one of claims 1-3, that comprises:
 - a heavy chain CDR1 sequence that has at least 80% sequence identity with the sequence DYAMH; and
 - a heavy chain CDR2 sequence GISWNSGSIVYADSVKG; and
 - a heavy chain CDR3 sequence that has at least 80% sequence identity with the sequence AVSGYYPYFDY; and
 - a light chain CDR1 sequence KSSQSVLYSSNNKNYLG; and
 - a light chain CDR2 sequence that has at least 85% sequence identity with the sequence WASTRES; and
 - a light chain CDR3 sequence QYYTTP.

5. An antibody or functional part or functional equivalent according to any one of claims 1-4, that comprises:
- a heavy chain CDR1 sequence DYAMH or DYAMY; and
 - a heavy chain CDR2 sequence GISWNSGSIVYADSVKG; and
 - 5 - a heavy chain CDR3 sequence AVSGYYPYFDY or AVSGYFPYFDY or AVSGYYPYFHY or AVSGYFPYFHY; and
 - a light chain CDR1 sequence KSSQSVLYSSNNKNYLG; and
 - a light chain CDR2 sequence WASTRES or WASIRES; and
 - a light chain CDR3 sequence QQYYTTP.
- 10 6. An antibody or functional part or functional equivalent according to any one of claims 1-5, comprising a heavy chain variable region sequence having at least 80% sequence identity with the sequence
- EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGISW
NSGSIVYADSVKGRFTISRDNKNSLYLQLNSLRAEDTAFYYCAKAVSGYYPYFD
15 YWGQGILVTVSS.
7. An antibody or functional part or functional equivalent according to any one of claims 1-6, comprising a light chain variable region sequence having at least 80% sequence identity with the sequence
- DIVMTQSPDLSVSLGERATINCKSSQSVLYSSNNKNYLGWYQQKPGQPPKLLIY
20 WASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYTTPSTFGQGTRL
EIK.
8. An antibody or functional part or function equivalent according to any one of claims 1-7 comprising:
- a heavy chain variable region sequence
 - 25 EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGIS
WNSGSIVYADSVKGRFTISRDNKNSLYLQLNSLRAEDTAFYYCAKAVSGYYP
YFDYWGQGILVTVSS, or
 - EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMYWVRQAPGKGLEWVSGIS
WNSGSIVYADSVKGRFTISRDNKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP
30 YFDYWGQGILVTVSS or
 - EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGIS
WNSGSIVYADSVKGRFTISRDNKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP
35 YFDYWGQGILVTVSS or
 - EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGIS
WNSGSIVYADSVKGRFTISRDNKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP

- YFHYWGQGILVTVSS or
 EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMYWVRQAPGKGLEWVSGIS
 WNSGSIVYADSVKGRFTISRDNANKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP
 YFDYWGGQGILVTVSS or
 5 EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMYWVRQAPGKGLEWVSGIS
 WNSGSIVYADSVKGRFTISRDNANKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP
 YFDYWGGQGILVTVSS or
 EVQVVESGGGLVQPGRSLRLSCAASGFTFDDYAMYWVRQAPGKGLEWVSGIS
 WNSGSIVYADSVKGRFTISRDNANKNSLYLQLNSLRAEDTAFYYCAKAVSGYFP
 10 YFHYWGQGILVTVSS and/or
- a light chain variable region sequence
 DIVMTQSPDSLVSFLGERATINCKSSQSVLYSSNNKNYLGWYQQKPGQPPKLL
 IWASTRESGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCQQYYTTPSTFGQG
 TRLEIK or
 15 DIVMTQSPDSLVSFLGERATINCKSSQSVLYSSNNKNYLGWYQQKPGQPPKLL
 IWASIRESGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCQQYYTTPSTFGQG
 TRLEIK.
9. An antibody or functional part or functional equivalent according to any one of
 claims 1-8, that is a human antibody or functional part or functional equivalent
 20 thereof.
 10. An antibody or functional part or functional equivalent according to any one of
 claims 1-9, that is able to bind melanoma cells, colon carcinoma cells, pancreas
 carcinoma cells and esophagus carcinoma cells.
 11. An antibody or functional part or functional equivalent according to any one of
 25 claims 1-10, wherein said antibody is of the IgG isotype, preferably IgG1 or IgG3.
 12. An antibody or functional part or functional equivalent according to claim 11
 comprising an arginine at amino acid position 345.
 13. An isolated, synthetic or recombinant antibody or functional part or functional
 equivalent thereof that competes with antibody AT14-012 for binding to amino acids
 30 K169, D171, V172, L173 and F176 of the CD9 sequence as depicted in Figure 2.
 14. An antibody or functional part or functional equivalent according to any one of
 claims 1-13, that is coupled to another compound.
 15. An antibody or functional part or functional equivalent according to claim 14,
 wherein said other compound is a detectable label, a chemotherapeutic drug, a toxic

- moiety, an immunomodulatory molecule, another CD9-specific binding compound, or a radioactive compound.
16. An isolated, recombinant or purified CD9 peptide with a length of at most 60 amino acid residues, wherein said peptide comprises at least 6 amino acid residues that are identical to at least 6 amino acid residues located within CD9 amino acid positions 169-176 as depicted in Figure 2.
17. An isolated, recombinant or purified CD9 peptide according to claim 16, that comprises amino acids corresponding to K169, D171, V172, L173 and F176 of the CD9 sequence as depicted in Figure 2.
18. An isolated, recombinant or purified CD9 peptide according to claim 16 or 17, that further comprises an amino acid corresponding to F176 of the CD9 sequence as depicted in Figure 2.
19. An isolated, synthetic or recombinant nucleic acid molecule with a length of at least 15 nucleotides, or a functional equivalent thereof, encoding at least one CDR sequence of an antibody or functional part or functional equivalent according to any one of claims 1-15.
20. A nucleic acid molecule or functional equivalent according to claim 19, that encodes at least the heavy chain CDR 1-3 and the light chain CDR 1-3 sequences of an antibody or functional part or functional equivalent according to any one of claims 1-15.
21. A nucleic acid molecule or functional equivalent according to claim 19 or 20, that encodes at least the heavy chain variable region sequence and/or the light chain variable region sequence of an antibody or functional part or functional equivalent according to any one of claims 1-15.
22. A nucleic acid molecule or functional equivalent according to any one of claims 19-21, comprising a sequence that has at least 80% sequence identity with a sequence selected from the group consisting of:
- gat tat gcc atg cac; and
 - ggt att agt tgg aat agt ggt agc ata gtc tat gcg gac tct gtg aag ggc; and
 - gcc gtg agt ggt tat tat ccc tac ttt gac tac; and
 - aag tcc agc cag agt gtt tta tac agc tcc aac aat aag aac tac tta ggt; and
 - tgg gca tct acc cgg gaa tcc; and
 - . cag caa tat tat act act cct.
23. A nucleic acid molecule or functional equivalent according to any one of claims 19-22, comprising a sequence that has at least 80% sequence identity with the sequence

- gaa gtg cag gtg gtg gag tct ggg gga ggc ttg gta cag cct ggc agg tcc ctg aga ctc tcc tgt
gca gcc tct gga ttc acc ttt gat gat tat gcc atg cac tgg gtc cgg caa gct cca ggg aag ggc ctg
gag tgg gtc tca ggt att agt tgg aat agt ggt agc ata gtc tat gcg gac tct gtg aag ggc cga
ttc acc atc tcc aga gac aac gcc aag aac tcc ctg tat ctg caa ctg aac agt ctg aga gct gag
5 gag acg gcc ttc tat tac tgt gca aaa gcc gtg agt ggt tat tat ccc tac ttt gac tac tgg ggc cag
gga att ttg gtc acc gtc tcc tca, and/or comprising a sequence that has at least 80%
sequence identity with the sequence gac atc gtg atg acc cag tct cca gac tcc ctg tct gtg
tct ctg ggc gag agg gcc acc atc aac tgc aag tcc agc cag agt gtt tta tac agc tcc aac aat
aag aac tac tta ggt tgg tac cag cag aaa cca gga cag cct cct aag ctg ctc att tac tgg gca
10 tct acc cgg gaa tcc ggg gtc cct gac cga ttc agt ggc agc ggg tct ggg aca gat ttc act ctc acc
atc agc agc ctg cag gct gaa gat gtg gca gtt tat tac tgt cag caa tat tat act act cct tcc acc
ttc ggc caa ggg aca cga ctg gag att aaa.
24. A nucleic acid molecule or functional equivalent thereof, encoding an antibody or
functional part or functional equivalent according to any one of claims 1-15.
- 15 25. A nucleic acid molecule according to any one of claims 19-24, that comprises cDNA,
peptide nucleic acid (PNA), locked nucleic acid (LNA), or a DNA/RNA helix.
26. A nucleic acid molecule according to any one of claims 19-25, that is codon optimized
for expression in a non-human host cell.
27. A vector comprising a nucleic acid molecule or functional equivalent according to any
20 one of claims 19-26.
28. An isolated or recombinant cell, or a non-human animal, comprising a nucleic acid
molecule or functional equivalent according to any one of claims 19-26 or a vector
according to claim 27.
29. A composition comprising an antibody or functional part or functional equivalent
25 according to any one of claims 1-15, or a nucleic acid molecule or functional
equivalent according to any one of claims 19-26, or a vector according to claim 27, or
a cell according to claim 28.
30. A composition according to claim 29, wherein said composition is a pharmaceutical
composition that also comprises a pharmaceutically acceptable carrier, diluent or
30 excipient.
31. A kit of parts comprising an antibody or functional part or functional equivalent
according to any one of claims 1-15, a nucleic acid molecule or functional equivalent
according to any one of claims 19-26, a vector according to claim 27 or a cell
according to claim 28 and a therapeutic agent useful in the treatment and/or

- prevention of a disorder associated with CD9-expressing cells, preferably a CD9 positive cancer.
32. The kit of parts according to claim 31, wherein said agent is an agent capable of stimulating C3 convertase formation or capable of counteracting inhibition of C3 convertase formation.
33. The kit of parts according to claim 32, wherein said agent is a CD55 blocking antibody, a CD46 blocking antibody or a CD59 blocking antibody, preferably a CD55 blocking antibody.
34. The kit of parts according to claim 31, wherein said agent is a blocking antibody specific for a co-inhibitory T cell molecule.
35. The kit of parts according to claim 34, wherein said antibody is selected from the group consisting of an anti-CTLA4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-SIRP α antibody, an anti-TIM3 antibody, an anti-LAG3 antibody, an anti-CD276 antibody, an anti-CD272 antibody, an anti-KIR antibody, an anti-A2AR antibody, an anti-VISTA antibody and an anti-IDO antibody, and preferably is a PD1 blocking antibody or a PDL1 blocking antibody.
36. An antibody or functional part or functional equivalent according to any one of claims 1-15, or a nucleic acid molecule or functional equivalent according to any one of claims 19-26, or a vector according to claim 27, or a cell according to claim 28, for use as a medicament or prophylactic agent.
37. An antibody or functional part or functional equivalent according to any one of claims 1-15, or a nucleic acid molecule or functional equivalent according to any one of claims 19-26, or a vector according to claim 27, or a cell according to claim 28, for use in a method for at least in part treating or preventing a disorder associated with CD9-expressing cells.
38. An antibody or functional part or functional equivalent according to any one of claims 1-15 for use in diagnosis of a disorder associated with CD9-expressing cells.
39. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 37 or 38, wherein said disorder is selected from the group consisting of CD9 positive cancer, osteoporosis, arthritis, lung inflammation, COPD, colitis, and a disorder associated with innate lymphoid cells.
40. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 39, wherein said CD9 positive cancer is selected from the group consisting of melanoma, colorectal

- cancer, pancreatic cancer, esophageal cancer, lung cancer, breast cancer, ovarian cancer, stomach cancer, squamous cell carcinoma, AML, multiple myeloma, gastric cancer, liver cancer, brain cancer, Kaposi sarcoma, carcinoma mucoepidermoid, choriocarcinoma, fibrosarcoma, cervical carcinoma, glioma, adenocarcinoma, lung adenocarcinoma, non-small-cell lung carcinoma, bladder cancer and small cell lung cancer.
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41. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to any one of claims 38-40 whereby said antibody or functional part or functional equivalent or nucleic acid
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- molecule or functional equivalent or vector or cell is combined with a therapeutic agent useful in the treatment and/or prevention of a disorder associated with CD9-expressing cells, preferably a CD9 positive cancer.
42. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 41 wherein said
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- agent is an agent capable of stimulating C3 convertase formation or capable of counteracting inhibition of C3 convertase formation.
43. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 42 wherein said
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- agent is a CD55 blocking antibody, a CD46 blocking antibody or a CD59 blocking antibody, preferably a CD55 blocking antibody.
44. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 41 wherein said
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- agent is a blocking antibody specific for a co-inhibitory T cell molecule.
45. An antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell for use according to claim 44 wherein said
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- antibody is selected from the group consisting of an anti-CTLA4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-SIRP α antibody, an anti-TIM3 antibody, an anti-LAG3 antibody, an anti-CD276 antibody, an anti-CD272 antibody, an anti-KIR antibody, an anti-A2AR antibody, an anti-VISTA antibody and an anti-IDO antibody, and preferably is a PD1 blocking antibody or a PDL1 blocking antibody.
46. Use of an antibody or functional part or functional equivalent according to any one of claims 1-15 for determining whether a sample comprises CD9-expressing cells.
47. Use according to claim 46, for determining whether a sample comprises CD9-expressing tumor cells.
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48. A method for determining whether CD9-expressing cells are present in a sample comprising:
- contacting said sample with an antibody or functional part or functional equivalent according to any one of claims 1-15, and
 - 5 - allowing said antibody or functional part or functional equivalent to bind CD9-expressing cells, if present, and
 - determining whether or not CD9-expressing cells are bound to said antibody or functional part or functional equivalent, thereby determining whether or not CD9-expressing cells are present in said sample.
- 10 49. A method according to claim 48, wherein said CD9 expressing cells are CD9 positive tumor cells.
50. A method for producing an antibody or functional part or functional equivalent according to any one of claims 1-15, the method comprising providing a cell with a nucleic acid molecule or functional equivalent or a vector according to any one of
- 15 claims 19-27, and allowing said cell to translate said nucleic acid molecule or functional equivalent or vector, thereby producing said antibody or functional part or functional equivalent according to any one of claims 1-15, the method preferably further comprising harvesting, purifying and/or isolating said antibody or functional part or functional equivalent according to any one of claims 1-15.
- 20 51. A method for at least in part treating and/or preventing a disorder associated with CD9-expressing cells, comprising administering to an individual in need thereof a therapeutically effective amount of an antibody or functional part or functional equivalent according to any one of claims 1-15, or a nucleic acid molecule or functional equivalent according to any one of claims 19-26, or a vector according to
- 25 claim 27, or a cell according to claim 28, or a composition according to claim 29 or 30.
52. A method according to claim 51 wherein said disorder is selected from the group consisting of CD9 positive cancer, osteoporosis, arthritis, lung inflammation, COPD, colitis, and a disorder associated with innate lymphoid cells.
53. A method according to claim 52, wherein said CD9 positive cancer is selected from
- 30 the group consisting of melanoma, colorectal cancer, pancreatic cancer, esophageal cancer, lung cancer, breast cancer, ovarian cancer, stomach cancer, squamous cell carcinoma, AML, multiple myeloma, gastric cancer, liver cancer, brain cancer, Kaposi sarcoma, carcinoma mucoepidermoid, choriocarcinoma, fibrosarcoma, cervical carcinoma, glioma, adenocarcinoma, lung adenocarcinoma, non-small-cell
- 35 lung carcinoma, bladder cancer and small cell lung cancer.

54. A method according to any one of claims 51-53 whereby said antibody or functional part or functional equivalent or nucleic acid molecule or functional equivalent or vector or cell is combined with a therapeutic agent useful in the treatment and/or prevention of a disorder associated with CD9-expressing cells, preferably a CD9 positive cancer.
55. A method according to claim 54 wherein said agent is an agent capable of stimulating C3 convertase formation or capable of counteracting inhibition of C3 convertase formation.
56. A method according to claim 55 wherein said agent is a CD55 blocking antibody.
57. A method according to claim 54 wherein said agent is a blocking antibody specific for a co-inhibitory T cell molecule.
58. A method according to claim 57 wherein said antibody is selected from the group consisting of an anti-CTLA4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-SIRP α antibody, an anti-TIM3 antibody, an anti-LAG3 antibody, an anti-CD276 antibody, an anti-CD272 antibody, an anti-KIR antibody, an anti-A2AR antibody, an anti-VISTA antibody and an anti-IDO antibody, and preferably is a PD1 blocking antibody or a PDL1 blocking antibody.
59. An *ex vivo* method for determining whether an individual is suffering from a CD9-positive cancer, the method comprising:
- contacting tumor cells from said individual with an antibody or functional part or functional equivalent according to any one of claims 1-15,
 - allowing said antibody or functional part or functional equivalent to bind CD9-expressing cells, if present, and
 - determining whether or not CD9-expressing cells are bound to said antibody or functional part or functional equivalent, thereby determining whether or not said individual is suffering from a CD9-positive cancer.
60. An antibody according to any one of claims 1-15, or an antibody for use according to any one of claims 36-45, or a use according to claims 46 or 47, or a method according to any one of claims 48-59, wherein said antibody is antibody AT14-012 or a functional part or functional equivalent thereof.
61. An isolated, synthetic or recombinant nucleic acid molecule, or a functional equivalent thereof, encoding a CD9 peptide according to any one of claims 16-18.
62. A vector comprising a nucleic acid molecule or functional equivalent according to claim 61.

63. A host cell comprising a nucleic acid molecule or functional equivalent according to claim 61, and/or a vector according to claim 62.
64. Use of a CD9 peptide according to any one of claims 16-18, or a nucleic acid molecule or functional equivalent according to claim 61, or a vector according to claim 62, for
5 producing, binding, detecting and/or obtaining an immune cell and/or an antibody, or a functional part or functional equivalent thereof, that is specific for CD9.
65. A method for producing a CD9-specific immune cell or a CD9-specific antibody, the method comprising immunizing a non-human animal with a CD9 peptide according to any one of claims 16-18 or with a nucleic acid molecule or functional equivalent
10 according to claim 61 or with a vector according to claim 62.
66. A method according to claim 65, further comprising harvesting a CD9-specific immune cell or antibody from said non-human animal.
67. An antibody or immune cell obtainable by a method according to claim 65 or 66.
68. An immunogenic composition comprising a CD9 peptide according to any one of
15 claims 16-18, or a nucleic acid molecule or functional equivalent according to claim 61 or a vector according to claim 62.
69. A diagnostic kit comprising a CD9 peptide according to any one of claims 16-18 and means for detecting antibody-bound or immune cell-bound CD9 peptides.
70. A CD9 peptide according to any one of claims 16-18 or a nucleic acid molecule or
20 functional equivalent according to claim 61 or a vector according to claim 62 for use as a medicament or prophylactic agent.
71. A CD9 peptide according to any one of claims 16-18 or a nucleic acid molecule or functional equivalent according to claim 61 or a vector according to claim 62 for use in immunotherapy.
- 25 72. A CD9 peptide according to any one of claims 16-18 for use as a diagnostic agent.