Claims

1. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of binding H3N2 and H7N7, comprising:

- a heavy chain CDR1 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 1, 3 and 4, and
- a heavy chain CDR2 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 6, 8 and 9, and
- a heavy chain CDR3 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 11, 13 and 14, and
- a light chain CDR1 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 16, 18 and 19, and
- a light chain CDR2 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 21, 23 and 24, and
- a light chain CDR3 sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's: 26, 28 and 29.

2. An isolated, synthetic or recombinant antibody or functional part or immunoglobulin chain or functional equivalent according to claim 1, having an *in vitro* H3N2 influenza A virus neutralizing activity with an IC50 value of less than 1 μg/ml.

3. An antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-2, having a heavy chain sequence comprising a sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's:31, 33 and 34 and/or having a light chain sequence which is at least 70% identical to a sequence selected from the group consisting of SEQ ID NO's:36, 38 and 39.

4. 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 thereof or immunoglobulin chain or functional equivalent according to any one of claims 1-3.

5. A nucleic acid molecule or a functional equivalent according to claim 4, comprising a sequence which has at least 70% sequence identity to a sequence selected from the group consisting of:

- SEQ ID NO's: 41, 43 and 44, and
- SEQ ID NO's: 46, 48 and 49, and
- SEQ ID NO's: 51, 53 and 54, and
- SEQ ID NO's: 56, 58 and 59, and
- SEQ ID NO's: 61, 63 and 64, and
- SEQ ID NO's: 66, 68 and 69.

6. A nucleic acid molecule or a functional equivalent according to claim 4 or 5, comprising a sequence which has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO's: 71, 73 and 74 and/or comprising a sequence which has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO's: 76, 78 and 79.

7. A vector comprising a nucleic acid molecule or functional equivalent according to any one of claims 4-6.

8. An isolated or recombinant cell comprising a nucleic acid molecule or functional equivalent according to any one of claims 4-6, and/or a vector according to claim 7.

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9. A pharmaceutical composition comprising an antibody or functional part or immunoglobulin chain or functional equivalent or a nucleic acid molecule or functional equivalent or a vector according to any one of claims 1-7 and a pharmaceutical acceptable carrier, diluent and/or excipient.

10. An antibody or functional part or immunoglobulin chain or functional equivalent or a nucleic acid molecule or functional equivalent thereof or a vector according to any one of claims 1-7, for use as a medicament and/or prophylactic agent.

11. An antibody or functional part or immunoglobulin chain or functional equivalent, or a nucleic acid molecule or functional equivalent, or a vector according to any one of claims 1-7, for use as a medicament and/or prophylactic agent for at least in part treating and/or preventing an influenza A virus infection.

12. A method for producing an antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3, comprising providing a cell with a nucleic acid molecule or functional equivalent or a vector according to any one of claims 4-7, and allowing said cell to translate said nucleic acid molecule or functional equivalent or vector, thereby producing said antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3, preferably further comprising harvesting, purifying and/or isolating said antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3.

13. An antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3 for use in diagnosis of an influenza A virus infection.

14. A method for determining whether an influenza A virus is present in a sample comprising:

- contacting said sample with an antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3,

- allowing said antibody or functional part or immunoglobulin chain or functional equivalent to bind said influenza A virus, if present, and
- determining whether influenza A virus is bound to said antibody or functional part or immunoglobulin chain or functional equivalent, thereby determining whether an influenza A virus is present in said sample.

15. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent thereof, capable of binding H3N2 and H7N7, said multimeric antibody or multimeric immunoglobulin or functional equivalent comprising:
i) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005; and
ii) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,
wherein said antibody selected in i) is different from said antibody selected in ii).

16. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15, comprising:
i) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005; and
ii) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,
wherein said antibody selected in i) is different from said antibody selected in ii).

17. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15 or 16, comprising:
i) the heavy chain sequence and the light chain sequence of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005, or a sequences that is at least 70% identical thereto; and
ii) the heavy chain sequence and the light chain sequence of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005, or a sequence that is at least 70% identical thereto,
wherein said antibody selected in i) is different from said antibody selected in ii).

18. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 17, comprising:
i) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of antibody AT10_002; and
ii) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of antibody AT10_005.

19. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15 or 16, comprising:
i) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of antibody AT10_002; and
ii) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of antibody AT10_005.

20. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-19, comprising:
i) the heavy chain sequence and the light chain sequence of antibody AT10_002, or sequences that are at least 70% identical thereto; and
ii) the heavy chain sequence and the light chain sequence of antibody AT10_005, or sequences that are at least 70% identical thereto.

21. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-20, which is a dimeric antibody.

22. An isolated or recombinant cell or a pharmaceutical composition comprising a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21.

23. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use as a medicament and/or prophylactic agent.

24. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use as a medicament and/or prophylactic agent for at least in part treating and/or preventing and/or alleviating the symptoms of an influenza A infection.

25. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use in diagnosis of an influenza A infection.

26. Use of a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 and/or a cell or pharmaceutical composition according to claim 22 in the manufacture of a medicament for the treatment and/or prevention of an influenza A virus infection.

27. Use of a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 in the manufacture of a medicament for the neutralization of a H1N1 influenza A virus and/or an H3N2 influenza A virus, wherein said H1N1 influenza A virus and/or said H3N2 influenza A virus is to be contacted with a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21, resulting in neutralization of said virus.

28. A method for determining whether an influenza A virus is present in a sample comprising:
- contacting said sample with a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21,
- allowing said multimeric antibody, multimeric immunoglobulin or functional equivalent to bind said influenza A virus, if present, and
- determining whether influenza A virus is bound to said multimeric antibody, multimeric immunoglobulin or functional equivalent, thereby determining whether an influenza A virus is present in said sample.

29. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of interacting with amino acids at positions A21, A324, A325, A327, B12, B14, B15, B16, B17, B18, B19, B25, B26, B30, B31, B32, B33, B34, B35, B36, B38, B146, B150, B153, and B154 of influenza A virus group 2 hemagglutinin (H3/H7).

30. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of interacting with amino acids at positions A38, A48, A275, A276, A277, A278, A289, A291, A318, B19, B20, B21, B36, B38, B39, B41, B42, B45, B46, B48, B49, B50, B52, B53, B56, B57, B58, B150 of influenza A virus group 2 hemagglutinin (H3/H7).

Claims

1. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of binding H3N2 and H7N7 and having an in vitro H3N2 influenza A virus neutralizing activity with an IC50 value of less than 1 μg/ml, comprising:

the heavy and light chain CDRs1-3 as defined by SEQ ID NO: 4, 9, 14, 19, 24 and 29, respectively; or sequences showing at least 85% identity thereto; or

the heavy and light chain CDRs1-3 as defined by SEQ ID NO: 3, 8, 13, 18, 23 and 28, respectively; or sequences showing at least 85% identity thereto; or

the heavy and light chain CDRs1-3 as defined by SEQ ID NO: 1, 6, 11, 16, 21 and 26, respectively, or sequences showing at least 85% identity thereto.

2. An isolated, synthetic or recombinant antibody or functional part or immunoglobulin chain or functional equivalent according to claim 1, having an in vitro H3N2 influenza A virus neutralizing activity with an IC50 value of less than 0.7 μg/ml.

3. An antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-2, having a heavy chain sequence comprising a sequence which is at least 85% identical to a sequence selected from the group consisting of SEQ ID NO's:31, 33 and 34 and/or having a light chain sequence which is at least 85% identical to a sequence selected from the group consisting of SEQ ID NO's:36, 38 and 39.

4. 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 thereof or immunoglobulin chain or functional equivalent according to any one of claims 1-3.

5. A nucleic acid molecule or a functional equivalent according to claim 4, comprising a sequence which has at least 85% sequence identity to a sequence selected from the group consisting of:

- SEQ ID NO's: 41, 43 and 44, and
- SEQ ID NO's: 46, 48 and 49, and

- SEQ ID NO's: 51, 53 and 54, and
- SEQ ID NO's: 56, 58 and 59, and
- SEQ ID NO's: 61, 63 and 64, and
- SEQ ID NO's: 66, 68 and 69.

6. A nucleic acid molecule or a functional equivalent according to claim 4 or 5, comprising a sequence which has at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NO's: 71, 73 and 74 and/or comprising a sequence which has at least 85% sequence identity to a sequence selected from the group consisting of SEQ ID NO's: 76, 78 and 79.

7. A vector comprising a nucleic acid molecule or functional equivalent according to any one of claims 4-6.

8. An isolated or recombinant cell comprising a nucleic acid molecule or functional equivalent according to any one of claims 4-6, and/or a vector according to claim 7.

9. A pharmaceutical composition comprising an antibody or functional part or immunoglobulin chain or functional equivalent or a nucleic acid molecule or functional equivalent or a vector according to any one of claims 1-7 and a pharmaceutical acceptable carrier, diluent and/or excipient.

10. An antibody or functional part or immunoglobulin chain or functional equivalent or a nucleic acid molecule or functional equivalent thereof or a vector according to any one of claims 1-7, for use as a medicament and/or prophylactic agent.

11. An antibody or functional part or immunoglobulin chain or functional equivalent, or a nucleic acid molecule or functional equivalent, or a vector according to any one of claims 1-7, for use as a medicament and/or prophylactic agent for at least in part treating and/or preventing an influenza A virus infection.

12. A method for producing an antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3, comprising providing a cell with a nucleic acid molecule or functional equivalent or a vector according to any one of claims 4-7, and allowing said cell to translate said nucleic acid molecule or functional equivalent or vector, thereby producing said antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3, preferably further comprising harvesting, purifying and/or isolating said antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3.

13. An antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3 for use in diagnosis of an influenza A virus infection.

14. A method for determining whether an influenza A virus is present in a sample comprising:
- contacting said sample with an antibody or functional part or immunoglobulin chain or functional equivalent according to any one of claims 1-3,
- allowing said antibody or functional part or immunoglobulin chain or functional equivalent to bind said influenza A virus, if present, and
- determining whether influenza A virus is bound to said antibody or functional part or immunoglobulin chain or functional equivalent, thereby determining whether an influenza A virus is present in said sample.

15. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent thereof, capable of binding H3N2 and H7N7, said multimeric antibody or multimeric immunoglobulin or functional equivalent comprising:
i) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005; and
ii) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,
wherein said antibody selected in i) is different from said antibody selected in ii),

and wherein

the AT10_001 heavy and light chain CDRs1-3 are defined by SEQ ID NO: 4, 9, 14, 19, 24 and 29, respectively; or sequences showing at least 85% identity thereto;

the AT10_002 heavy and light chain CDRs1-3 are defined by SEQ ID NO: 3, 8, 13, 18, 23 and 28, respectively; or sequences showing at least 85% identity thereto;

the AT10_004 heavy and light chain CDRs1-3 are defined by SEQ ID NO: 1, 6, 11, 16, 21 and 28, respectively, or sequences showing at least 85% identity thereto;

the AT10_005 heavy and light chain CDRs1-3 are defined by SEQ ID NO: 5, 10, 15, 20, 25 and 30, respectively, or sequences showing at least 85% identity thereto.

16. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15, comprising:

i) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005; and

ii) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,

wherein said antibody selected in i) is different from said antibody selected in ii).

17. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15 or 16, comprising:

i) the heavy chain sequence and the light chain sequence of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,; and

ii) the heavy chain sequence and the light chain sequence of an antibody selected from the group consisting of AT10_001 and AT10_002 and AT10_004 and AT10_005,

wherein said antibody selected in i) is different from said antibody selected in ii),

and wherein

the AT10_001 heavy and light chain sequences are defined by SEQ ID NO: 34 and 39, respectively; or sequences showing at least 85% identity thereto;

the AT10_002 heavy and light chain sequences are defined by SEQ ID NO: 33 and 38, respectively; or sequences showing at least 85% identity thereto;

the AT10_004 heavy and light chain sequences are defined by SEQ ID NO:31 and 36, respectively, or sequences showing at least 85% identity thereto; and

the AT10_005 heavy and light chain sequences are defined by SEQ ID NO: 35 and 40, respectively, or sequences showing at least 85% identity thereto.

18. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 17, comprising:

i) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of antibody AT10_002; and
ii) at least two different heavy chain CDR sequences and at least two different light chain CDR sequences of antibody AT10_005.

19. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to claim 15 or 16, comprising:
i) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of antibody AT10_002; and
ii) heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 sequences of antibody AT10_005.

20. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-19, comprising:
i) the heavy chain sequence and the light chain sequence of antibody AT10_002, or sequences that are at least 85% identical thereto; and
ii) the heavy chain sequence and the light chain sequence of antibody AT10_005, or sequences that are at least 85% identical thereto.

21. A multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-20, which is a dimeric antibody.

22. An isolated or recombinant cell or a pharmaceutical composition comprising a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21.

23. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use as a medicament and/or prophylactic agent.

24. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use as a medicament and/or prophylactic agent for at least in part treating and/or preventing and/or alleviating the symptoms of an influenza A infection.

25. A synthetic or recombinant multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 for use in diagnosis of an influenza A infection.

26. Use of a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 and/or a cell or pharmaceutical composition according to claim 22 in the manufacture of a medicament for the treatment and/or prevention of an influenza A virus infection.

27. Use of a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21 in the manufacture of a medicament for the neutralization of a H1N1 influenza A virus and/or an H3N2 influenza A virus, wherein said H1N1 influenza A virus and/or said H3N2 influenza A virus is to be contacted with a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21, resulting in neutralization of said virus, and wherein said multimeric antibody, multimeric immunoglobulin or functional equivalent comprises at least one of antibodies AT10_004 and AT10_005, and at least one of antibodies AT10_001, AT10_002 and AT10_004, or functional equivalents thereof.

28. A method for determining whether an influenza A virus is present in a sample comprising:

- contacting said sample with a multimeric antibody, multimeric immunoglobulin or functional equivalent according to any one of claims 15-21,
- allowing said multimeric antibody, multimeric immunoglobulin or functional equivalent to bind said influenza A virus, if present, and
- determining whether influenza A virus is bound to said multimeric antibody, multimeric immunoglobulin or functional equivalent, thereby determining whether an influenza A virus is present in said sample.

29. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of interacting with amino acids at positions A21, A324, A325, A327, B12, B14, B15, B16, B17, B18, B19, B25, B26, B30, B31, B32, B33, B34, B35, B36, B38, B146, B150, B153, and B154 of influenza A virus group 2 hemagglutinin (H3/H7).

30. An isolated, synthetic or recombinant antibody or functional part thereof, or immunoglobulin chain or functional equivalent thereof, capable of interacting with amino acids at positions A38, A48, A275, A276, A277, A278, A289, A291, A318, B19, B20, B21, B36, B38, B39, B41, B42, B45, B46, B48, B49, B50, B52, B53, B56, B57, B58, B150 of influenza A virus group 2 hemagglutinin (H3/H7).