

capsid (N) protein is considered the major diagnostic antigen. WO2005/118813 discloses a variant of SARS-CoV-1-related S protein and the detection of its presence, or the presence of antibodies binding to it, in samples. US2006/0188519 discloses peptides for the diagnosis of a SARS-CoV-1 infection. Hsueh *et al.* reported that IgG could be detected as early as four days after the onset of a SARS-CoV-1 infection, simultaneously as or one day *earlier* than IgM and IgA (Hsue, P. R., Huang, L. M., Chen, P. J., Kao, C. L., and Yang P. C. (2004) Chronological evolution of IgM, IgA, IgG and neutralization antibodies after infection with SARS-associated coronavirus, Clinical Microbiology and Infection, 10(12), 1062-1066). Reusken *et al.* disclose the specific, but not necessarily sensitive detection of antibodies to a SARS-CoV-2 spike protein fragment (Specific serology for emerging human coronaviruses by protein microarray. Euro Surveill. 2013;18(14). Yu *et al.* (2020) Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhu, China, Microbes and Infection 22 (2020), 74-79 disclose, without pointing to specific antigens, that immunological methods may be used for detecting a SARS-CoV-2 infection, but are associated with poor sensitivity and specificity.

The above-discussed problems are solved by the present invention, as described in the present specification and in the claims.

Summary

In one aspect, the present disclosure provides a method for aiding in the diagnosis of ~~diagnosing a~~ SARS-CoV-2 infection comprising the step of detecting the presence or absence of an IgA class antibody to SEQ ID NO1, ~~preferably IgA class antibody~~, in a blood sample from a subject. In another aspect, the present disclosure provides a method for aiding in the diagnosis of a SARS-CoV-2 infection comprising the step of detecting the presence of an IgA and an IgG and an IgM class antibody to SEQ ID NO1 in a blood sample from a subject, ~~the differential diagnosis of a coronavirus infection, preferably for distinguishing between a SARS-CoV; preferably SARS-CoV-2; MERS, NL63, 229E, OC43 and HKU1 infection, comprising the step of detecting the presence or absence of an antibody to SEQ ID NO1 in a sample from a subject, preferably an IgA and/or IgG class antibody, more preferably an IgA class antibody.~~

In yet another aspect, the present disclosure provides a use of an IgA class antibody to SEQ ID NO1, ~~preferably IgA class antibody, for diagnosing a~~ for aiding in the diagnosis of a SARS-CoV-2 infection at an early stage, which is 5 or fewer days after the onset of disease symptoms, in a blood sample from a subject wherein the subject is likely to suffer from a SARS-CoV-2 infection if the presence of an IgA class antibody to SEQ ID NO1 or the presence of an IgA and an IgG and an IgM class antibody to SEQ ID NO1 in the blood sample from the subject, ~~or for the differential diagnosis of a coronavirus infection, preferably for distinguishing between a SARS-CoV, preferably SARS-CoV-2, MERS and NL63, 229E, OC43 and HKU1 infection.~~

In a further aspect, the present disclosure provides a use of a kit ~~comprising a polypeptide comprising SEQ ID NO1 or a variant thereof, preferably coated to a diagnostically useful carrier and one or more, preferably all reagents from the group comprising an antibody to SEQ ID NO1, a washing buffer, a~~ means for detecting in a blood sample from a mammalian, preferably human, patient, an antibody to SEQ ID NO1 at an early stage of the infection, which is 5 or fewer days after the onset of disease symptoms, wherein the kit comprises a means for detecting the presence of an IgA class antibody to SEQ ID NO1 or for detecting the presence of an IgA and an IgM and an IgG class antibody to SEQ ID NO1 and a polypeptide comprising SEQ ID NO1 or a variant thereof, using a competitive assay, a capture bridge assay, an immunometric assay, a class-specific second antibody on the solid phase, or a direct or indirect class capture assay, wherein the polypeptide comprising a variant of SEQ ID NO1

a) consists of the full length-sequence of SEQ ID NO1 fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, or b) comprises a variant which is a truncated SEQ ID NO1, i. e. less than the full-length sequence of SEQ ID NO1, wherein the truncation is at the N-terminus, C-terminus or both, optionally fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, and (i) comprises a fragment of SEQ ID NO1 comprising at least 25, 50, 75, 100, 150, 200, 250, 300, 400, 500 or 600 successive amino acids of SEQ ID NO1 and/or (ii) comprises a fragment of SEQ ID NO1 comprising at least 200 successive amino acids with an identity to the reference fragment of SEQ ID NO1 of at least 80, 85, 90, 92, 94, 95, 96, 97, 98, 99 %, and wherein the variant has the ability to bind to an antibody to SEQ ID NO1 from a sample from a patient suffering from SARS-CoV-2. ~~the presence of antibody to SEQ ID NO1, preferably an IgA class antibody, preferably a secondary antibody binding specifically to IgA class antibodies, preferably comprising a detectable label, and a dilution buffer.~~

~~In yet another aspect, the present disclosure provides a use of a polypeptide comprising SEQ ID NO1 or a variant thereof or an antibody to SEQ ID NO1, preferably an IgA class antibody, for the manufacture of a diagnostic kit. In yet another aspect, the present disclosure provides a use of a recombinant antibody binding to SEQ ID NO1 which is preferably recognized by a secondary antibody binding to IgA class antibodies as a calibrator for the early diagnosis of a SARS-CoV-2 infection.~~

Detailed Description

In a first aspect, the invention provides a method for diagnosing a SARS-CoV-2 infection, comprising the step of detecting the presence or absence of an antibody to SEQ ID NO:1, preferably IgM, IgG and/or IgA class antibody, more preferably IgA class antibody, in a sample from a subject. Whenever reference to a SEQ ID NO is made throughout this specification and the SEQ ID NO denotes an amino acid sequence, it is intended to denote a polypeptide comprising said corresponding amino acid string even if in that connection the term "polypeptide" is not specifically mentioned. The term "comprising" has two meanings in connection with this invention, namely "containing" and "consisting of."

In a second aspect, the invention provides a method for the differential diagnosis of a coronavirus infection, preferably for distinguishing between a SARS-CoV; preferably SARS-CoV-2; MERS, NL63, 229E, OC43 and HKU1 infection, comprising the step of detecting the presence or absence of an antibody to SEQ ID NO: 1 in a sample from a subject, preferably an IgA and/or IgG class antibody, more preferably an IgA class antibody.

In a preferred embodiment, the presence of an IgG and/or IgM class antibody to SEQ ID NO: 1 is detected in addition to an IgA class antibody to SEQ ID NO: 1.

In accordance with the present invention, the "subject", or interchangeably referred to herein as "patient", refers to a mammal, preferably a human, but may alternatively also refer to a different mammal, such as a non-human primate or other mammalian animal or even a non-mammalian animal capable of producing an antibody to SEQ ID NO: 1 or variant thereof.

In accordance with the present invention, the term "sample" from a subject may be a sample of any bodily fluid or tissue of said subject that may comprise an antibody. Exemplary bodily fluids include for example blood, saliva, nasal mucus or lymph fluid. In a preferred embodiment, the sample is a blood sample, preferably selected from the group comprising whole blood, serum, plasma, capillary blood, arterial blood, venous blood or any mixture thereof. The capillary blood is preferably in the form of a

Claims

1. A method for ~~diagnosing~~ aiding in the diagnosis of a SARS-CoV-2 infection comprising the step of detecting the presence or absence of an ~~antibody to SEQ ID NO1, preferably~~ IgA class antibody to SEQ ID NO1, in a blood sample from a subject.

~~2. A method for the differential diagnosis of a coronavirus infection, preferably for distinguishing between a SARS-CoV; preferably SARS-CoV-2; MERS, NL63, 229E, OC43 and HKU1 infection, comprising the step of detecting the presence or absence of an antibody to SEQ ID NO1 in a sample from a subject, preferably an IgA and/or IgG class antibody, more preferably an IgA class antibody.~~

~~3. The method according to any of claims 1 or 2, wherein the presence of an IgG and/or IgM class antibody to SEQ ID NO1 is detected in addition to an IgA class antibody to SEQ ID NO1.~~

~~4. The method according to any of claims 1 to 3, wherein the sample is a blood sample, preferably selected from the group comprising whole blood, serum or plasma.~~

~~5.2.~~ The method according to ~~any of claims 1 to 4~~ claim 1, wherein an IgA class antibody to SEQ ID NO1 is detected using a labeled secondary antibody, ~~preferably~~ binding to IgA class antibodies, preferably human IgA class antibodies.

~~3.~~ The method according to any of claims 1 to 2, wherein the subject is likely or more likely to suffer from a SARS-CoV-2 infection if an IgA antibody to SEQ ID NO1 is detected in the sample.

~~4.~~ A method for aiding in the diagnosis of a SARS-CoV-2 infection comprising the step of detecting the presence of an IgA and an IgG and an IgM class antibody to SEQ ID NO1 in a blood sample from a subject.

~~5.~~ The method according to claim 4, comprising the step of providing a diagnostically useful carrier coated with a polypeptide comprising SEQ ID NO1 or a variant thereof and a sample from a patient suspected of being infected with SARS-CoV-2 and contacting the carrier with the sample under conditions allowing for binding of any antibodies.

wherein the polypeptide comprising a variant of SEQ ID NO1

a) consists of the full length-sequence of SEQ ID NO1 fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, or

b) comprises a variant which is a truncated SEQ ID NO1, i. e. less than the full-length sequence of SEQ ID NO1, wherein the truncation is at the N-terminus, C-terminus or both, optionally fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, and

(i) comprises a fragment of SEQ ID NO1 comprising at least 25, 50, 75, 100, 150, 200, 250, 300, 400, 500 or 600 successive amino acids of SEQ ID NO1 and/or

(ii) comprises a fragment of SEQ ID NO1 comprising at least 200 successive amino acids with an identity to the reference fragment of SEQ ID NO1 of at least 80, 85, 90, 92, 94, 95, 96, 97, 98, 99 %,

and wherein the variant has the ability to bind to an antibody to SEQ ID NO1 from a sample from a patient suffering from SARS-CoV-2.

6. The method according to any of claims 4 to 5, wherein a capture bridge assay is used for detecting the presence of an IgA and an IgG and an IgM class antibody to SEQ ID NO1.

7. The method according to any of claims 4 to 6, wherein the subject is likely or more likely to suffer from a SARS-CoV-2 infection if the presence of an antibody from the group comprising an IgA class antibody and an IgG class antibody and an IgM class antibody to SEQ ID NO1 is detected in the sample.

6.8. The method according to any of claims 1 to 57, wherein ~~the IgA antibody is detected using~~ a method selected from the group comprising colorimetry, immunofluorescence, detection of enzymatic activity, chemiluminescence and radioactivity is used.

7.9. The method according to any of claims 1 to 68, wherein the infection is detected at an early stage, which is 5 or fewer days after the onset of disease symptoms.

8.10. A use of an ~~antibody to SEQ ID NO1, preferably IgA class antibody,~~ to SEQ ID NO1 for diagnosing-aiding in the diagnosis of a SARS-CoV-2 infection at an early stage, which is 5 or fewer days after the onset of disease symptoms, in a blood sample from a subject,

wherein the subject is likely to suffer from a SARS-CoV-2 infection if the presence of an IgA class antibody to SEQ ID NO1 or the presence of an IgA and an IgG and an IgM class antibody to SEQ ID NO1 is detected in the blood sample from the subject~~or for the differential diagnosis~~

~~of a coronavirus infection, preferably for distinguishing between a SARS-CoV, preferably SARS-CoV-2, MERS and NL63, 229E, OC43 and HKU1 infection.~~

~~9. The use according to claim 8, wherein the use is for the early diagnosis of a SARS-CoV-2 infection.~~

11. A use of a kit for detecting in a blood sample from a mammalian, preferably human, patient, an antibody to SEQ ID NO1 at an early stage of the infection, which is 5 or fewer days after the onset of disease symptoms,

wherein the kit comprises a means for detecting the presence of an IgA class antibody to SEQ ID NO1 or for detecting the presence of an IgA and an IgM and an IgG class antibody to SEQ ID NO1 and a polypeptide comprising SEQ ID NO1 or a variant thereof, using a competitive assay, a capture bridge assay, an immunometric assay, a class-specific second antibody on the solid phase, or a direct or indirect class capture assay

wherein the polypeptide comprising a variant of SEQ ID NO1

a) consists of the full length-sequence of SEQ ID NO1 fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, or

b) comprises a variant which is a truncated SEQ ID NO1, i. e. less than the full-length sequence of SEQ ID NO1, wherein the truncation is at the N-terminus, C-terminus or both, optionally fused to one or more from the group comprising an artificial linker, an affinity tag and another antigen, and

(i) comprises a fragment of SEQ ID NO1 comprising at least 25, 50, 75, 100, 150, 200, 250, 300, 400, 500 or 600 successive amino acids of SEQ ID NO1 and/or

(ii) comprises a fragment of SEQ ID NO1 comprising at least 200 successive amino acids with an identity to the reference fragment of SEQ ID NO1 of at least 80, 85, 90, 92, 94, 95, 96, 97, 98, 99 %,

and wherein the variant has the ability to bind to an antibody to SEQ ID NO1 from a sample from a patient suffering from SARS-CoV-2.

12. The use according to any of claims 10 to 11, wherein it is detected whether an IgA class antibody is present or absent.

13. The use according to any of claims 10 to 11, comprising detecting the presence of an antibody from the group comprising an IgA and an IgG and an IgM class antibody to SEQ ID NO1, preferably using a capture bridge assay.

14. The method or use according to any of claims 1 to 10, wherein the sample is a mammalian sample, preferably a human sample.

15. The method or use according to any of claims 1 to 14, wherein the sample is selected from the group comprising whole blood, serum or plasma.

16. The method or use according to any of claims 1 to 15, wherein the term "SARS-CoV-2" refers to a virus characterized by the genome deposited on GenBank under accession code MN908947 and derivatives thereof having at least 80, preferably 85, preferably 88, preferably 90, preferably 91, preferably 92, preferably 93, preferably 94, preferably 95, preferably 96, preferably 97, preferably 98, preferably 99, preferably 99.5, preferably 99.8, preferably 99.9 or 99.99 percent sequence identity over the entire genome nucleotide sequence.

~~10. A kit comprising a polypeptide comprising SEQ ID NO1 or a variant thereof, preferably coated to a diagnostically useful carrier and one or more, preferably all reagents from the group comprising an antibody to SEQ ID NO1, a washing buffer, a means for detecting the presence of antibody to SEQ ID NO1, preferably an IgA class antibody, preferably a secondary antibody binding specifically to IgA class antibodies, preferably comprising a detectable label, and a dilution buffer.~~

~~11. The kit according to claim 10, wherein the diagnostically useful carrier is selected from the group comprising a bead, preferably a paramagnetic bead, a test strip, a microtiter plate, a membrane, preferably from the group comprising western blot, line blot and dot blot, a lateral flow device, a glass surface, a slide, a microarray and a biochip and is preferably a microtiter plate.~~

~~12. The kit according to claim 10 or 11, wherein the kit comprises two or more, preferably three or more calibrators.~~

~~13. The kit according to claim 12, wherein each calibrator is a recombinant antibody binding to SEQ ID NO1 which is preferably recognized by a secondary antibody binding to IgA class antibodies.~~

~~14. A use of a polypeptide comprising SEQ ID NO1 or a variant thereof or an antibody to SEQ ID NO1, preferably an IgA class antibody, for the manufacture of a diagnostic kit.~~

~~15. A use of a recombinant antibody binding to SEQ ID NO1 which is preferably recognized by a secondary antibody binding to IgA class antibodies as a calibrator for the early diagnosis of a SARS-CoV-2 infection.~~