

Another problem underlying the present invention is to provide an assay for distinguishing an acute infection by Flaviviruses, in particular Zika virus, from a vaccination or a previous infection by the same or another Flavivirus, preferably dengue virus.

Another problem underlying the present invention is to provide a vaccine against a flavivirus, preferably Zika virus infection.

Another problem underlying the present invention is to provide a resource-efficient, yet diagnostically reliable test for distinguishing a flavivirus infection from another disease.

Another problem underlying the present invention is to provide a test that may be used during a longer time window between the initial exposure or the onset of symptoms and the day the sample for the diagnosis is obtained.

Another problem underlying the present invention is to provide a test for distinguishing between a primary Flavivirus infection, preferably with a Flavivirus other than the Zika virus, and a secondary Flavivirus infection, preferably Zika infection, which method is diagnostically more reliable than state of the art methods, in particular with regard to avoiding false positive or negative results, and may ideally be applied to samples from patients having an IgM deficiency.

Summary

The problem underlying the present invention is solved by the subject-matter of the attached independent and dependent claims.

In one aspect, the present disclosure refers to a kit comprising a diagnostically useful carrier, wherein the diagnostically useful carrier is a carrier comprising a means for specifically capturing an antibody that binds to SEQ ID NO.: 1 in a sample from a subject, and wherein the kit further comprises a means for specifically detecting a captured antibody, , and wherein the means for specifically detecting a captured antibody is a secondary antibody binding to the constant region of IgA class antibodies. In another aspect, the present disclosure refers to a kit comprising a diagnostically useful carrier and a polypeptide, wherein the diagnostically useful carrier comprises a means for specifically capturing all IgA class antibodies, which is an antibody binding to all IgA class antibodies, wherein the polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.:1 or a variant thereof, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1. In yet another aspect, the present

disclosure refers to a method of detecting the presence or absence of an antibody that binds to SEQ ID NO.: 1 in a sample from a subject, wherein the antibody is an IgA class antibody, the method comprising: a) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing the antibody that binds to SEQ ID NO.: 1; and detecting the captured antibody with a means for detecting the captured antibody, or b) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies and detecting whether the captured antibodies bind to SEQ ID NO.: 1 using a polypeptide, wherein the polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.: 1 or a variant thereof, wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.:1. In still another aspect, the present disclosure refers to an *in vitro* use of i) a kit as disclosed herein, or ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for the reduction of cross reactivity in the diagnosis of a Zika virus infection, wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1. In a further aspect, the present disclosure refers to an *in vitro* use of: i) a kit as disclosed herein, or ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA/IgM/IgG antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA/IgM/IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for distinguishing a primary Zika virus infection from a secondary Zika virus infection, wherein the use comprises detecting an IgA, IgM, and IgG class antibody that binds to SEQ ID NO.: 1, wherein the detection of an increase or decrease of an IgA or IgM class antibody that binds to SEQ ID NO.: 1 before the detection of the presence of an IgG class antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates the presence of a primary Zika virus infection, wherein the detection of an increase of an IgA class antibody that binds to SEQ ID NO.: 1 and the detection of an increase of an IgG class antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates the presence of a secondary Zika virus infection, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.

In yet another aspect, the present disclosure refers to an *in vitro* use of i) a kit as disclosed herein, or ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for increasing the reliability of the diagnosis of a Zika virus infection, wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1. In yet another aspect, the present disclosure refers to an *in vitro* of i) a kit as disclosed herein or ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for the diagnosis of a Zika virus infection, wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.

In a first example, the problem underlying the present invention is solved by a polypeptide comprising a sequence selected from the group comprising SEQ ID NO1, SEQ ID NO2, SEQ ID NO3, SEQ ID NO4, SEQ ID NO5, SEQ ID NO6, SEQ ID NO7, SEQ ID NO8, SEQ ID NO19 and SEQ ID NO9 or a variant thereof, preferably SEQ ID NO1 or a variant thereof, preferably a dimer and/or hexamer, more preferably a dimer, for the diagnosis of a disease.

In a second example, the problem is solved by a diagnostically useful carrier comprising a means for specifically capturing an antibody to SEQ ID NO1 in a sample from a subject.

In a preferred example, the carrier further comprises one or more than one means, which means is for specifically capturing an antibody to an antigen from the group comprising SEQ ID NO2, SEQ ID NO3, SEQ ID NO4, SEQ ID NO5, SEQ ID NO6, SEQ ID NO7, SEQ ID NO8, SEQ ID NO19 and SEQ ID NO9.

In a preferred example, the carrier is selected from the group comprising a bead, preferably a paramagnetic particle, a test strip, a microtiter plate, a blot, preferably from the group comprising western blot, line blot and dot blot, lateral flow test, a glass surface, a slide, a biochip and a membrane, and is preferably a bead a line blot or microtiter plate, more preferably a microtiter plate.

In a third example, the problem is solved by a kit comprising the diagnostically useful carrier according to the present disclosure, optionally as well as a means for specifically detecting a captured antibody.

Claims

1. A kit comprising a diagnostically useful carrier, wherein the diagnostically useful carrier is a carrier comprising a means for specifically capturing an antibody that binds to SEQ ID NO.: 1 in a sample from a subject, and wherein the kit further comprises a means for specifically detecting a captured antibody, and wherein the means for specifically detecting a captured antibody is a secondary antibody binding to the constant region of IgA class antibodies.
2. A kit comprising a diagnostically useful carrier and a polypeptide, wherein the diagnostically useful carrier comprises a means for specifically capturing all IgA class antibodies, which is an antibody binding to all IgA class antibodies, wherein the polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.:1 or a variant thereof, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.
3. A method of detecting the presence or absence of an antibody that binds to SEQ ID NO.: 1 in a sample from a subject, wherein the antibody is an IgA class antibody, the method comprising:
 - a) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing the antibody that binds to SEQ ID NO.: 1; and detecting the captured antibody with a means for detecting the captured antibody, or
 - b) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies and detecting whether the captured antibodies bind to SEQ ID NO.: 1 using a polypeptide, wherein the polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.: 1 or a variant thereof, wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.:1.
4. The method according to claim 3, wherein the sample is a blood or CSF sample.

5. The method according to claim 3 or 4, further comprising detecting the presence or absence of an antibody that binds to SEQ ID NO.:1, wherein the antibody is an IgM and/or IgG class antibody, wherein the method further comprises:
- 5 c) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing the antibody that binds to SEQ ID NO.: 1; and
detecting the captured antibody with a means for detecting the captured antibody, or
d) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing all IgM or IgG class antibodies and detecting whether the captured antibodies bind to SEQ ID NO.: 1 using a polypeptide, wherein the
10 polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.:1 or a variant thereof, wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.:1.
6. The kit or method according to any of claims 1 to 5, wherein the carrier is selected
15 from the group comprising: a bead; a test strip, a microtiter plate, a blot; lateral flow test, a glass surface, a slide, a biochip and a membrane.
7. The method according to any of claims 3 to 6, wherein the detecting of the presence or absence of an antibody that binds to SEQ ID NO.: 1 and the presence or absence
20 of an antibody to one or more further antigens is detected in spatially separate binding reactions.
8. The method according to any of claims 3 to 7, further comprising a step of monitoring the captured IgA, IgM and/or IgG class antibodies for a time period of at least three
25 days, after the step of detecting whether the captured antibodies bind to SEQ ID NO.: 1.
9. The method according to any of claims 3 to 8, further comprising detecting the total concentration of an IgM antibody that binds to SEQ ID NO.: 1, wherein the method
30 further comprises:
- e) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing the IgM antibody that binds to SEQ ID NO.: 1, and
detecting the captured IgM antibody with a means for detecting the captured IgM antibody, or
35 f) contacting the sample with a diagnostically useful carrier comprising a means for specifically capturing all IgM class antibodies and the captured IgM antibodies and detecting whether the captured antibodies bind to SEQ ID NO.: 1 using a polypeptide,

wherein the polypeptide is a recombinant polypeptide comprising a sequence as set out in SEQ ID NO.: 1 or a variant thereof, wherein the variant of the polypeptide has the ability to bind specifically to an IgM antibody that binds to SEQ ID NO.: 1.

- 5 10. The kit or method according to any of claims 1 to 9, wherein the antibody is a mammalian antibody.
11. The kit according to any of claims 1, 2, and 10, wherein the kit comprises a secondary antibody binding to the constant region of IgG class antibodies.
- 10 12. The kit according to any of claims 1, 2, and 10 to 11, wherein the kit comprises a secondary antibody binding to the constant region of IgM class antibodies.
13. The kit according to any of claims 1, 2, and 10 to 12, further comprising one or more from the group comprising a sample dilution buffer, a washing buffer and a buffer comprising a means for detecting any specifically captured antibody, a chemical solution for carrying out a detection reaction, a positive control, a negative control and a standard solution comprising a SEQ ID NO.: 1-binding antibody for preparing a calibration curve.
- 15 14. An *in vitro* use of
- 20 i) a kit according to any of claims 1, 2, 6, and 10 to 13, or
- 25 ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or
- 30 iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for the reduction of cross reactivity in the diagnosis of a Zika virus infection, wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.
- 35 15. An *in vitro* use of:
- i) a kit according to any of claims 1, 2, 6, and 10 to 13, or

- ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA/IgM/IgG antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or
- iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA/IgM/IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof,
- for distinguishing a primary Zika virus infection from a secondary Zika virus infection, wherein the use comprises detecting an IgA, IgM, and IgG class antibody that binds to SEQ ID NO.: 1,
- wherein the detection of an increase or decrease of an IgA or IgM class antibody that binds to SEQ ID NO.: 1 before the detection of the presence of an IgG class antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates the presence of a primary Zika virus infection,
- wherein the detection of an increase of an IgA class antibody that binds to SEQ ID NO.: 1 and the detection of an increase of an IgG class antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates the presence of a secondary Zika virus infection, and
- wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.
16. An *in vitro* use of
- i) a kit according to any of claims 1, 2, 6, and 10 to 13, or
- ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or
- iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for increasing the reliability of the diagnosis of a Zika virus infection,
- wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and
- wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.
17. The kit, method or use according to any of claims 1 to 16, wherein the antibody is detected using a method selected from the group comprising immunodiffusion techniques, immunoelectrophoretic techniques, light scattering immunoassays,

agglutination techniques, labeled immunoassays such as those from the group comprising radiolabeled immunoassay, enzyme immunoassays such as colourimetric assays, chemiluminescence, immunoassays and immunofluorescence techniques.

5 18. An *in vitro* use of

i) a kit according to any of claims 1, 2, 6, and 10 to 13 or

ii) a diagnostically useful carrier comprising a means for specifically capturing an IgA antibody that binds to SEQ ID NO.: 1, and a means for detecting the captured antibody; or

10 iii) a diagnostically useful carrier comprising a means for specifically capturing all IgA class antibodies, and a polypeptide comprising SEQ ID NO.: 1 or a variant thereof, for the diagnosis of a Zika virus infection,

wherein the detection of the presence of an IgA antibody that binds to SEQ ID NO.: 1 in a sample from a subject indicates increased likelihood of a subject suffering from a Zika virus infection, and

15 wherein the variant of the polypeptide has the ability to bind specifically to an antibody that binds to SEQ ID NO.: 1.

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