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

In a first aspect, the problem is solved by a diagnostically useful carrier comprising a eukaryotic cell overexpressing an adult ACh receptor and a eukaryotic cell overexpressing a fetal ACh receptor, wherein the cell is fixed for immunofluorescence. In an example, there is disclosed a diagnostically useful carrier comprising a eukaryotic cell overexpressing an adult ACh receptor or a variant thereof and a eukaryotic cell overexpressing a fetal ACh receptor or a variant thereof, wherein the cell is fixed for immunofluorescence.

In a preferred example, any eukaryotic cell overexpressing an autoantigen, preferably from the group comprising an adult ACh receptor, a fetal ACh receptor and Musk, is pre-fixed.

In a preferred example, the carrier further comprises a eukaryotic cell overexpressing Musk or a variant thereof.

In a preferred example, the cell overexpressing an adult ACh receptor or a variant thereof and the cell overexpressing a fetal ACh receptor or a variant thereof permanently express adult and fetal ACh receptor, respectively.

In a preferred example, the carrier further comprises a control, preferably a mock-transfected cell.

In a preferred example, the cell is selected from the group comprising HEK293, HeLa, CHO and Jurkat cells and derivatives thereof.

In a preferred example of the carrier, at least one eukaryotic cell, preferably all eukaryotic cells overexpressing an autoantigen from the group comprising adult ACh receptor, fetal ACh receptor and Musk or a variant thereof comprises or comprise one or more vectors, wherein the nucleic acid encoding the autoantigen is under the control of an promotor inducible by addition of an inducer, and wherein for each cell an additional, spatially separate eukaryotic cell is present which comprises the same vector lacking said nucleic acid or comprises the same vector, but does not express the autoantigen, preferably because of the absence of the inducer.

In a second aspect, the disclosure relates to a method for the detection of an autoantibody to ACh receptor, optionally in addition to detecting an autoantibody to Musk, comprising the steps:

autoantibody to ACh receptor, optionally in addition to detecting an autoantibody to Musk, comprising the steps:

a) contacting the sample with the carrier according to the present disclosure under conditions allowing formation of a complex comprising an autoantibody from the group comprising an autoantibody to ACh receptor, preferably adult and/or fetal ACh receptor, and Musk and an autoantigen from the group comprising ACh receptor and Musk,

b) contacting any complex formed in step b) with a fluorescent ligand to the autoantibody,

c) removing any fluorescent ligand not bound to an autoantibody, and

d) detecting the presence or absence of the fluorescent ligand.

In a third aspect, the problem is solved by a kit comprising the carrier according to the present disclosure and a ligand to an autoantibody to ACh receptor, optionally also to Musk, wherein the ligand is a fluorescent ligand, wherein any eukaryotic cell overexpressing an autoantigen is preferably pre-fixed.

In a fourth aspect, the problem is solved by use of the combination of a eukaryotic cell overexpressing an adult ACh receptor and a eukaryotic cell overexpressing a fetal ACh receptor for increasing the sensitivity of an immunofluorescence assay for the detection of an autoantibody to ACh receptor. In one example, there is disclosed a use of the combination of a eukaryotic cell overexpressing an adult ACh receptor or a variant thereof and a eukaryotic cell overexpressing a fetal ACh receptor or a variant thereof for increasing the sensitivity of an assay, preferably immunofluorescence assay, for the detection of an autoantibody to ACh receptor.

In a preferred example, the presence or absence of a fluorescent ligand binding to the autoantibody indicates whether or not the autoantibody is present in the sample.

In a preferred example, the use is for diagnosing an autoimmune disease, preferably myasthenia gravis, Lambert-Eaton-Myasthenia syndrome (LEMS) and other muscular disorders OMD.

In a preferred example, the eukaryotic cell expressing an adult ACh receptor or a variant thereof and the eukaryotic cell overexpressing a fetal ACh receptor or a variant thereof and optionally the eukaryotic cell expressing Musk or a variant thereof are spatially separated.

Claims

1. A diagnostically useful carrier comprising a eukaryotic cell overexpressing an adult ACh receptor and a eukaryotic cell overexpressing a fetal ACh receptor, wherein the cell is fixed for immunofluorescence.

2. The diagnostically useful carrier according to claim 1, wherein any eukaryotic cell overexpressing an autoantigen is pre-fixed.

3. The diagnostically useful carrier according to any of claims 1 to 2, wherein the carrier further comprises a eukaryotic cell overexpressing Musk represented by SEQ ID NO. 13 or a variant thereof, wherein the variant comprises at least 80% sequence identity to SEQ ID NO. 13 and is able to bind to an autoantibody to Musk.

4. The diagnostically useful carrier according to any of claims 1 to 3, wherein the cell overexpressing an adult ACh receptor and the cell overexpressing a fetal ACh receptor permanently express adult and fetal ACh receptor, respectively.

5. The diagnostically useful carrier according to any of claims 1 to 4, wherein the carrier further comprises a control, preferably a mock-transfected cell.

6. The diagnostically useful carrier according to any of claims 1 to 5, wherein the cell is selected from the group comprising HEK293, HeLa, CHO and Jurkat cells and derivatives thereof.

7. The diagnostically useful carrier according to any of claims 1 to 6,

wherein at least one eukaryotic cell, preferably all eukaryotic cells overexpressing an autoantigen from the group comprising adult ACh receptor, fetal ACh receptor and Musk represented by SEQ ID NO.13 or a variant thereof comprises or comprise one or more vectors, wherein the nucleic acid encoding the autoantigen is under the control of an promotor inducible by addition of an inducer,

and wherein for each cell an additional spatially separate eukaryotic cell is present which comprises the same vector lacking said nucleic acid or comprises the same vector, but does not express the autoantigen, preferably because of the absence of the inducer,

wherein the variant comprises at least 80% sequence identity to SEQ ID NO. 13 and is able to bind to an autoantibody to Musk.

8. A method for the detection of an autoantibody to ACh receptor, optionally in addition to detecting an autoantibody to Musk, comprising the steps:

    a) contacting the sample with the carrier according to any of claims 1 to 7 under conditions allowing formation of a complex comprising an autoantibody from the group comprising an autoantibody to ACh receptor, preferably adult and/or fetal ACh receptor, and Musk and an autoantigen from the group comprising ACh receptor and Musk,

    b) contacting any complex formed in step b) with a fluorescent ligand to the autoantibody,

    c) removing any fluorescent ligand not bound to an autoantibody, and

    d) detecting the presence or absence of the fluorescent ligand.

9. A kit comprising the carrier according to any of claims 1 to 7 and a ligand to an autoantibody to ACh receptor, optionally also to Musk, wherein the ligand is a fluorescent ligand, wherein any eukaryotic cell overexpressing an autoantigen is preferably pre-fixed.

10. Use of the combination of a eukaryotic cell overexpressing an adult ACh receptor and a eukaryotic cell overexpressing a fetal ACh receptor for increasing the sensitivity of an immunofluorescence assay for the detection of an autoantibody to ACh receptor.

11. The use according to claim 10, wherein the presence or absence of a fluorescent ligand binding to the autoantibody indicates whether or not the autoantibody is present in a sample.

12. The carrier according to any one of claims 1 to 7, the method according to claim 8 or the use according to any of claims 10 to 11, wherein the eukaryotic cell expressing an adult ACh receptor and the eukaryotic cell overexpressing a fetal ACh receptor and optionally the eukaryotic cell expressing Musk represented by SEQ ID NO. 13 or a variant thereof are spatially separated, wherein the variant comprises at least 80% sequence identity to SEQ ID NO13 and is able to bind to an autoantibody to Musk.

13. The carrier according to any one of claims 1 to 7 and 12, the method according to claim 8 or 12 or the use according to any of claims 10 to 12, wherein the eukaryotic cell overexpressing an adult ACh receptor and a eukaryotic cell overexpressing a fetal ACh receptor and optionally the eukaryotic cell expressing Musk represented by SEQ ID NO13 or a variant thereof are colocalized, wherein the variant comprises at least 80% sequence identity to SEQ ID NO13 and is able to bind to an autoantibody to Musk.

14. The carrier according to any one of claims 1 to 7, 12 and 13, the method according to any one of claims 8, 12 and 13 or the use according to any of claims 10 to 13, wherein the sample comprises antibodies from a patient, preferably blood, more preferably selected from the group comprising serum, liquor, plasma and whole blood.

15. The carrier according to any one of claims 1 to 7 and 12 to 14, the method according to any one of claims 8 and 12 to 14 or the use according to any of claims 10 to 14,

wherein the carrier, method or use is for the diagnosis of myasthenia gravis, Lambert-Eaton-Myasthenia syndrome (LEMS) and other muscular disorders (OMD).