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(71) .Applicant; 000236436
Hamamatsu Photonics K.K.
1126-1, Ichinocho, Kamamatsu-shi, Shizuoka-ken
(72) Inventor; Masataka Jibu
c/o Hamamatsu Photonics K.K,
1126-1, Ichinocho, Hamamatsu-shi, Shizuoka-ken
(72) Inventor; Kaoru Sakatani
YinHua DongLu, HepingLi, Beijing,
The People's Republic of China 100029
(74) Agent; Patent Attorney,
Yoshiki Hasegawa (and another four)

(54) [Title of the Invention,]

NEAR- INFRARED RAY FLUORESCENT TRACER AND FLUORESCENCE IMAGING METHOD

(57) [Abstract]

[Problem to be Solved]

The invention provides a near-infrared ray fluorescent tracer and fluorescence imaging method.

[Solution]

A near-infrared ray fluorescent tracer involving the present invention comprises a complex of at least a near-infrared ray fluorescent pigment and a substance that contains fat-soluble ingredients, furthermore comprises a detection target identifying part. Furthermore the near-infrared ray fluorescent tracer is such that the near-infrared ray fluorescent pigment is indocyanine green pigments and the substance that contains a fat-soluble ingredient is a high density lipoprotein. Moreover, the near-infrared ray fluorescent tracer is such that the detection target identifying part is antibodies.

In an ex vivo fluorescence imaging method of the present invention, the near-infrared ray fluorescent tracer is introduced into a living body, the living body is irradiated with excitation light, and the near-infrared ray fluorescent

[Claims for the Patent]

[Claim l]

A near-infrared ray fluorescent tracer comprising a complex of at least near-infrared ray fluorescent pigments and a substance that contains a fat--soluble ingredient.

[Claim 2]

A near-infrared ray fluorescent tracer comprising at least a near- infrared ray fluorescent pigment, a substance that contains a fat-soluble ingredient, and a detection target identifying part.

[Claim 3]

The near-infrared ray fluorescent tracer according to claim 1 or 2, wherein

the near-infrared ray fluorescent pigment is indocyanine green pigment and the substance that contains a fat-soluble ingredient is a high density lipoprotein,

[Claim 4]

The near-infrared ray fluorescent tracer according to claim 2 or 3, wherein

the detection target identifying part is antibodies.

[Claim 5]

An ex vivo fluorescence imaging method comprising:

introducing the near-infrared ray fluorescent tracer of any of claims 1 to 4 into a living body;

irradiating the living body with excitation light; and

detecting near-infrared ray fluorescent light from the near-infrared ray fluorescent tracer.

[Detailed Description of the Invention]

[0001]

[Field of the Invention]

The present invention relates to a near-infrared ray fluorescent tracer.

[0002]

[Prior Art]

Methods in which ex vivo measurements of an internal part of thick living sample (a human body for instance) performed using light are important in medical research and in diagnosis and treatment of diseases. Knowing in advance the position and size of the tumors in particular using image diagnosis is an important technique for extracting tumors, and several methods are well-known.

[0003]

However, the image diagnosis of nerve axonal flow and tumor tissue using radioactive isotopes (RI) has problems such as worries about exposure and contamination, and the problem is the management is complex. Also, since this cannot be used outside controlled areas, the application in an operating time is difficult, posing problems. For instance, substance is

which actively transport the substance from the nerve endings towards the cell body (nerve axonal flow, if the speed of the nerve axonal flow is slower than normal, it is known that it is possible to diagnose that the nerve cells have been damaged in some way. There have been actual attempts to perform this type of diagnosis using an RI as the substance, but it has the similar problems as tumor diagnosis.

[0004] Moreover, Regarding X ray CT techniques, the issue of being exposed to radiation is the same as the case of radioisotopes. Another problem is that, since the devices used are large and a test subject must be positioned deep within a tomography device, there also exists issues in that it is difficult to apply these techniques during surgery,

[0005]

[Problems to be Solved by the Invention]

The present invention has been executed in view of the above-described problems. Specifically, it provides a novel tracer having a low toxicity which can be used against the living body for extracorporeally measuring the inner state of a living body sample having thickness (such as human body) with near-infrared ray fluorescence. It also provides an extracorporeal measuring and imaging method using the tracer.

[0006]

[Means for Solving the Objective Problem]

It is thought that since near-infrared ray light is highly permeable to the living body, a pigment emitting the near-infrared ray light is allowed to be distributed within the body and its extracorporeal measurement can be carried out for application to a variety of diagnoses and others. Further, this method can be accomplished by the configuration of only small and inexpensive devices such as a halogen lamp, CCD camera, optical filter and a lens etc.

[0007]

On the other hand, the pigment poses a problem of toxicity when it is used as a tracer in the living body, and the pigments that can be used are limited. In view of this toxicity problem, indocyanine green has actually been put to use in clinical application as one that can be used as a tracer pigment.

The pigment discharges near red fluorecent light (835nm) in organic solvent, and there is an instance in which using this, blood vessels at the bottom of the eye was observed fluorecently.

[0008]

However, though the pigment is fluorescent in a non-polar solvent (such as an organic solvent), the pigment is non-fluorescent in a polar solvent (such as an aqueous solution), and in an unaltered form the pigment described above

The inventor diligently researched the above-described points, and succeeded in discovering a new near-infrared ray fluorescent tracer that contains a non-toxic near-infrared ray fluorescent pigment and is water soluble.

That is, the inventor discovered that when a pigment, such as indocyanine green pigment, that is low in toxicity but substantially non- fluorescent in aqueous solution, forms a complex with an appropriate high-density lipoprotein or the like, it was fluorescent. Based on this discovery, the inventor succeeded in making the complex described above as a near-infrared ray fluorescent tracer. The inventor also discovered a near-infrared ray fluorescent pigment tracer further with an identifying part capable of uniquely identifying a detection target. Based on this discovery, the inventor succeeded in making the complex into a near-infrared ray fluorescent tracer capable of uniquely identifying the detection target.

[0010]

More specifically, the present invention provides a near-infrared ray fluorescent tracer comprising a complex that contains at least a near- infrared fluorescent pigment and R substance that contains a fat-soluble ingredient.

[0011]

The present invention also provides a near-infrared ray fluorescent tracer comprising at least a near-infrared ray fluorescent pigment, a substance that contains a fat-soluble ingredient, and a detection target identifying part.

[0012]

Furthermore, the present invention provides a near-infrared ray fluorescent tracer wherein the near-infrared ray fluorescent pigment is an indocyanine green pigment and the substance that contains a fat-soluble ingredient is a high-density lipoprotein.

[0013]

The present invention further provides a near-infrared ray fluorescent tracer wherein the detection target identifying part is an antibody.

[0014]

Furthermore, this invention provides an extracorporeal fluorescent imaging method comprising introducing a near-infrared ray fluorescent tracer into a living body, irradiating the living body with an excitation light and detecting near-infrared ray fluorescence from the tracer.

[0015]

The following embodiments are provided for a more detailed description of the present invention.

[0016]

[Embodiments of the Invention]

(Near-infrared ray tracer invention) The near-infrared ray tracer of the present invention contains a pigment that has fluorescent wavelengths in the near-infrared ray band, and that is traceable through a detection of the fluorescence. Here, the near-infrared ray band should be at least 700nm, more preferably 800 nm or more of the range, and the upper limit is not

necessary that it has fluorescence in the medium where the target detection object exists, but as explained in the following it is not always necessary to be fluorescent in water soluble liquid.

[0017]

Moreover, Since the tracer of the present invention is to be used inside a living body, particularly required characteristics for the tracer include solubility in water (so as to dissolve in vivo liquid medium), and being non-toxic to the living body. As long as the pigment combines the characteristics described above, in the present invention, there are no other restrictions on the pigment. A pigment such as indocyanine green pigment can be used favorably. Indocyanine green pigment is water soluble. Also, indocyanine green is used as liver circulatory function detection test drug, and so toxicity does not present a problem.

[0018]

The near-infrared ray tracer according to this invention is preferably a complex with the pigment bonded to other living ingredient. Among the other living ingedients which can be bonded by the pigment, there are no particular restrictions and various biological components can be selected depending on the application of the tracer according to the invention. For example, (i) when the pigment described above is insoluble in an in vivo liquid medium (e.g., blood or spinal fluid), complexes with different living substances can be formed to make the pigment soluble; (ii) conversely, in spite of the fact that the pigment described above is soluble in the in vivo liquid medium (e.g., blood or spinal fluid), but in case that is not sufficiently fluorescent in an aqueous in vivo liquid medium, and rather becomes fluorescent in a non-aqueous medium, it is possible to make the pigment fluorescent by allowing the pigment to form complexes with different living ingredient, (iii) Further, as described below, to introduce a part for uniquely identifying the detection target to the tracer of the present invention, a complex can be formed with an appropriate biological ingredient.

[0019]

Actually, the above-described indocyanine pigment does not present any problem in terms of toxicity, but is substantially non-fluorescent in aqueous solution. Therefore, as shown in the embodiment of the present invention, indocyanine pigment is enabled to form a complex of the indocyanine pigment and a high-density lipoprotein that is a biological component having a fat-soluble ingredient, thereby made to contain indocyanine pigment which is made fluorescent.

[0020]

Furthermore, the near-infrared ray tracer of the present invention is preferably made to be a complex of the above-described pigment and has the part that uniquely identifies the detection target. The identifying part is

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