In the present technology, the non-demented control (NDC) subject includes healthy humans, and means the subjects which may have any diseases but not have cognitive dysfunction diseases (non-demented control).

Also in the present technology, when referring to collectively as cognitive dysfunction diseases, it is intended that mild cognitive impairment (MCI), Alzheimer's disease (AD), and dementia-type neurological diseases are also included. In the present technology, mild cognitive impairment (MCI) and Alzheimer's disease (AD) can preferably be detected.

The peptides identified in the present technology have significance as biomarkers when detected not only in serum but also in other biological samples such as blood, serum, plasma, cerebrospinal fluid, urine, and the like. Similarly, source proteins from which the aforementioned peptides are derived (hereinafter referred to as "intact proteins") or source peptides also have a significance as biomarkers.

[0018]

Thus, in one aspect, the present technology provides one or more biomarkers for detecting cognitive dysfunction diseases selected from the following (a), (b), and (c):

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and,

(c) a biomarker for detecting cognitive dysfunction diseases

consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof.

[0019]

In another aspect, t~~T~~he present technology provides a method for detecting cognitive dysfunction diseases in which one or more biomarkers for detecting cognitive dysfunction diseases selected from the aforementioned (a) biomarker, (b) biomarker, and (c) biomarker in a biological sample are measured simultaneously or separately.

[0020]

In a further aspect, t~~T~~he present technology provides a kit for detecting cognitive dysfunction diseases for measuring one or more biomarkers for detecting cognitive dysfunction diseases selected from the aforementioned (a) biomarker, (b) biomarker, and (c) biomarker.

[0021]

In yet another aspect, th~~T~~he present technology provides a method for selecting a combination of multiple biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers comprising measuring two or more biomarkers for cognitive dysfunction diseases in a biological sample from a subject, conducting an analysis of the measurement results of each of the aforementioned two or more biomarkers by a logistic regression analysis, and selecting a combination of the biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers based on the results of the aforementioned analysis.

Advantageous Effects of Invention

CLAIMS:

1. One or more biomarkers for detecting cognitive dysfunction diseases selected from the following (a), (b), and (c):

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and

(c) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof.

2. A method for detecting cognitive dysfunction diseases comprising measuring one or more biomarkers for detecting cognitive dysfunction diseases selected from the following (a), (b), and (c) in a biological sample simultaneously or separately:

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and

(c) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof.

3. The method for detecting cognitive dysfunction diseases according to Claim 2 comprising measuring two biomarkers, namely, the (c) biomarker and the (a) biomarker or the (b) biomarker.

4. The method for detecting cognitive dysfunction diseases according to Claim 2 or 3 comprising measuring two biomarkers, namely, the (c) biomarker and the (a) biomarker when the detection of the cognitive dysfunction diseases is the detection of mild cognitive impairment or measuring two biomarkers, namely, the (c) biomarker and the (b) biomarker when the detection of the cognitive dysfunction diseases is Alzheimer's disease.

5. A cognitive dysfunction disease detection kit for measuring one or more biomarkers for detecting cognitive dysfunction diseases selected from the following (a), (b), and (c):

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and

(c) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof.

6. The cognitive dysfunction disease detection kit according to Claim 5 comprising an antibody against the biomarker or aptamer.

7. A method for selecting a combination of multiple biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers comprising:

measuring two or more biomarkers for cognitive dysfunction diseases in a biological sample from a subject;

conducting an analysis of the measurement results of each of the two or more biomarkers by a logistic regression analysis; and

selecting a combination of the biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers based on the results of the analysis.

CLAIMS:

1. A method for detecting cognitive dysfunction diseases comprising measuring a biomarker of (a) or (b) and a biomarker of (c):

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and

(c) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof.

2. The method for detecting cognitive dysfunction diseases according to Claim 1 comprising measuring two biomarkers, namely, a biomarker of the (a) and a biomarker of the (c) when the detection of the cognitive dysfunction diseases is the detection of mild cognitive impairment or measuring two biomarkers, namely, a biomarker of the (b) and a biomarker of the (c) biomarker when the detection of the cognitive dysfunction diseases is Alzheimer's disease.

3. A cognitive dysfunction disease detection kit for measuring a biomarker of the following (a) or (b) and a biomarker of the following (c) for detecting cognitive dysfunction diseases:

(a) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of apolipoprotein A1 comprising the amino acid sequence represented by SEQ ID NO:1 or a partial peptide thereof;

(b) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of transthyretin comprising the amino acid sequence represented by SEQ ID NO:2 or a partial peptide thereof; and,

(c) a biomarker for detecting cognitive dysfunction diseases consisting of an intact protein of complement C3 comprising the amino acid sequence represented by SEQ ID NO:3 or a partial peptide thereof;

4. The cognitive dysfunction disease detection kit according to Claim 3 comprising an antibody against the biomarker or aptamer.

5. A method for selecting a combination of multiple biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers comprising:

measuring two or more biomarkers for cognitive dysfunction diseases in a biological sample from a subject;

conducting an analysis of the measurement results of each of the two or more biomarkers by a logistic regression analysis; and

selecting a combination of the biomarkers for detecting cognitive dysfunction diseases which gives a high percentage of correct answers based on the results of the analysis.