



(12) **DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION**

(13) **A1**

(86) Date de dépôt PCT/PCT Filing Date: 2016/03/17
(87) Date publication PCT/PCT Publication Date: 2016/09/22
(85) Entrée phase nationale/National Entry: 2017/09/14
(86) N° demande PCT/PCT Application No.: EP 2016/055883
(87) N° publication PCT/PCT Publication No.: 2016/146783
(30) Priorité/Priority: 2015/03/17 (GB1504432.4)

(51) Cl.Int./Int.Cl. *C40B 40/10* (2006.01),
C12N 9/92 (2006.01), *C12Q 1/00* (2006.01),
C12Q 1/44 (2006.01), *C12Q 1/533* (2006.01),
C40B 30/04 (2006.01), *G01N 33/48* (2006.01),
G01N 33/53 (2006.01), *G01N 33/564* (2006.01),
G01N 33/573 (2006.01), *G01N 33/68* (2006.01),
C12N 9/16 (2006.01), *C07K 14/575* (2006.01)

(71) Demandeur/Applicant:
ELECTROPHORETICS LIMITED, GB

(72) Inventeurs/Inventors:
PIKE, IAN HUGO, GB;
RUSSELL, CLAIRE LOUISE, GB;
WARD, MALCOLM, GB

(74) Agent: BERESKIN & PARR LLP/S.E.N.C.R.L., S.R.L.

(54) Titre : **MATERIAUX ET PROCEDES POUR LE DIAGNOSTIC ET LE TRAITEMENT DE LA MALADIE D'ALZHEIMER**
(54) Title: **MATERIALS AND METHODS FOR DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE**

(57) **Abrégé/Abstract:**

Alzheimer's disease (AD) is the most common type of dementia in aging adults with the number of people living with AD projected to increase, making the search for treatments and tools to diagnose and measure disease progression increasingly urgent. In particular, ideal biomarkers for diagnosis of AD should not only have high specificity for disease versus non-disease and high sensitivity for distinguishing between disease types but also should be able to detect changes at a very early stage of the disease. Using microglia activation as an early event of AD's onset, the present inventors have identified a panel of biomarkers in CSF which has the potential to diagnose, stage and determine the likelihood of developing AD.

(51) **International Patent Classification:**
G01N 33/68 (2006.01) *C12N 9/92* (2006.01)
C07K 14/575 (2006.01)

(21) **International Application Number:**
PCT/EP2016/055883

(22) **International Filing Date:**
17 March 2016 (17.03.2016)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**
1504432.4 17 March 2015 (17.03.2015) GB

(71) **Applicant:** **ELECTROPHORETICS LIMITED**
[GB/GB]; Coveham House, Downside Bridge Road,
Cobham Surrey KT11 3EP (GB).

(72) **Inventors:** **PIKE, Ian Hugo**; Electrophoretics Limited,
Coveham House, Downside Bridge Road, Cobham Surrey
KT11 3EP (GB). **RUSSELL, Claire Louise**; Electrophor-
etics Limited, Coveham House, Downside Bridge Road,
Cobham Surrey KT11 3EP (GB). **WARD, Malcolm**; Elec-
trophoretics Limited, Coveham House, Downside Bridge
Road, Cobham Surrey KT11 3EP (GB).

(74) **Agents:** **BRYERS LLP** et al.; 7 Gay Street, Bath Bath and
North East Somerset BA1 2PH (GB).

(81) **Designated States** (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))*
- *of inventorship (Rule 4.17(iv))*

Published:

- *with international search report (Art. 21(3))*
- *with sequence listing part of description (Rule 5.2(a))*

(54) **Title:** MATERIALS AND METHODS FOR DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE

(57) **Abstract:** Alzheimer's disease (AD) is the most common type of dementia in aging adults with the number of people living with AD projected to increase, making the search for treatments and tools to diagnose and measure disease progression increasingly ur-
gent. In particular, ideal biomarkers for diagnosis of AD should not only have high specificity for disease versus non-disease and high sensitivity for distinguishing between disease types but also should be able to detect changes at a very early stage of the disease. Using microglia activation as an early event of AD's onset, the present inventors have identified a panel of biomarkers in CSF which has the potential to diagnose, stage and determine the likelihood of developing AD.

WO 2016/146783 A1

Materials and Methods for Diagnosis and Treatment of Alzheimer's Disease

Field of the Invention

The invention relates to biomarker panels and methods for diagnosing, staging and assessing the
5 likelihood of developing a neurocognitive disorder. In particular, the invention concerns biomarker
panels useful in methods for the diagnosis and treatment of Alzheimer's disease.

Background of the Invention

Alzheimer's disease (AD) is the most common type of dementia in aging adults with the number
of people living with AD projected to increase dramatically over the next few decades, making the
10 search for treatments and tools to diagnose and measure disease progression increasingly
urgent.

Approved treatments are few and of limited efficacy, serving mostly to slow or delay progression.
Currently there is no cure.

AD gives rise to an irreversible progressive loss of cognitive functions and of functional autonomy.
15 While the time it takes for AD to develop will vary from person to person, advanced signs include
severe memory impairment, confusion, language disturbances, impaired judgment, personality
and behaviour changes. Patients with AD may become non-communicative and hostile. As the
disease ends its course in profound dementia, patients are unable to care for themselves and
often require institutionalization or professional care in the home setting. While some patients
20 may live for many years after being diagnosed with AD, the average life expectancy after
diagnosis is eight years.

Although AD can only be definitively diagnosed by brain biopsy or upon autopsy after a patient
died, in clinical settings brain biopsy is rarely performed and diagnosis is still primarily made
based on the history of the symptoms and depends on a battery of neurological, psychometric
25 and biochemical tests, which include the measurement of biomarkers.

Nevertheless, these present methods are still not satisfactory in the diagnosing of AD and other
neurocognitive disorders at the early stage of the disease when potential therapies are more
likely to prevent or slow down neurodegeneration.

As the brain is in direct contact with the cerebrospinal fluid (CSF), and pathological changes in

the brain often result in altered biochemical composition of the CSF, this makes it an ideal source for biomarkers of neurocognitive disorders. In AD, currently three “core” CSF biomarkers (amyloid β 1-42, total tau and phosphorylated tau) are routinely used to diagnose AD. All three of these CSF biomarkers demonstrate high levels of sensitivity (falling within the 80-90% criteria specified by the National Institute of Neurological and Disorders and Stroke and the Alzheimer Disease and Related Disorders Work Group) but struggle to differentiate AD from other forms of dementia and neurological disorders. For example, CSF amyloid β 1-42 levels are decreased in AD but are also reportedly lower in Lewy body dementia (LBD), fronto-temporal dementia (FTD), vascular dementia (VaD), amyotrophic lateral sclerosis (ALS) and Creutzfeldt-Jakob disease (CJD) (Blennow K et al., Nat Rev Neurol. 2010,6:131-44). Similarly, total tau levels are raised in AD but are also found elevated following stroke, traumatic brain injury, FTD, VaD and CJD1.

Two key features of an ideal biomarker are high specificity for disease versus non-disease and high sensitivity to distinguish between disease types. In addition, biomarkers that reflect the pathological process of AD and that are able to detect changes at a very early stage of the disease, before degeneration is observed by brain imaging and neuropathological tests, are very sought after.

The ideal biomarker or biomarker panel would be the first indicator for starting treatment as early as possible, when degeneration is still limited, it would prove immensely valuable in screening the effectiveness of new therapies in clinical trial settings, particularly those trials that are focused on preventing the development of neuropathological changes. Such biomarker or biomarker panel would also be useful in the follow-up of the development of the disease.

Hence, there remains a need for biomarkers that may perform with superior sensitivity and/or specificity in the early diagnosis, staging and prognostic monitoring of patients with Alzheimer’s disease and other neurocognitive disorders.

25 **Summary of the Invention**

The present invention, therefore, provides novel biomarker panels for use in methods for diagnosing, staging and assessing the likelihood of developing a neurocognitive disorder, in particular Alzheimer’s disease.

In a first aspect, the present invention provides for a biomarker panel comprising:

- 30 i) phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
- ii) thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a

variant or a fragment thereof.

In one embodiment of this first aspect, the panel further comprises ubiquitin carboxy-terminal hydrolase L1 which comprises or has an amino acid sequence of SEQ ID NO:4 or an isoform or a variant or a fragment thereof; and/or vitamin D binding protein which comprises or has an amino acid sequence of SEQ ID NO: 5 or an isoform or a variant or a fragment thereof.

In another embodiment of this first aspect, the panel further comprises one or more biomarkers selected from a protein involved in a KEGG pathway wherein KEGG pathway is selected from the group of complement and coagulation cascade, or glycolysis/glycogenesis, or prion disease, or amino and nucleotide sugar metabolism, or antigen processing and presentation, or extracellular matrix-receptor interaction, or focal adhesion, or regulation of actin cytoskeleton or alanine/aspartate/glutamate metabolism.

In another embodiment of this aspect the panel further comprises at least one, optionally two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of this aspect, the panel further comprises at least two or more, optionally at least three or more biomarkers selected from the group of Dynactin subunit 1, Cofilin-1, Peroxiredoxin-1, MARCKS-related protein, Moesin, Actin, Protein TMSB4XP4, ApoE, Gelsolin, Secretogranin, Albumin and complement proteins.

In a second aspect, there is provided a method for diagnosing a neurocognitive disorder in a subject, the method comprising:

- a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to the first aspect and its embodiments;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether that subject has a neurocognitive disorder by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers.

In a third aspect, there is provided a method for staging a neurocognitive disorder in a subject, the method comprising:

- a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to the first aspect and its embodiments;
- b) measuring in said sample the concentration or the amount of each of the biomarkers

of said biomarker panel;

c) determining the stage of the neurocognitive disorder in said subject by comparing said concentration or amount of each of the biomarkers of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers.

5 In a fourth aspect the present invention provides for a method for assessing in a subject the likelihood of developing a neurocognitive disorder, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to the first aspect and its embodiments;

b) measuring in said sample the concentration or the amount of each of the biomarkers
10 of said biomarker panel;

c) determining whether that subject is likely to develop a neurocognitive disorder by comparing said concentration or amount of each of the biomarkers of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers.

In embodiments of these second, third and fourth aspects, the neurocognitive disorder is
15 characterised by microglia activation and/or is selected from the group of mild cognitive impairment, Alzheimer's disease, vascular dementia, dementia with lewy bodies, fronto-temporal dementia or combinations thereof.

In particular, the neurocognitive disorder is Alzheimer's disease.

In a fifth aspect of the present invention there is provided a method for treating Alzheimer's
20 disease in a subject, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to the first aspect and its embodiments;

b) measuring in said sample the concentration or the amount of each of the biomarkers
of said biomarker panel;

25 c) determining whether that subject has Alzheimer's disease by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations or amounts of said biomarkers;

d) administering to said subject an Alzheimer's disease treatment selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g.
30 Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof.

In a sixth aspect of the present invention there is provided a method for aiding the prognosis of a treatment for Alzheimer's disease in a subject, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to the first aspect and its embodiments;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

5 c) determining whether said treatment for Alzheimer's disease is successful by comparing said concentration or amount of each of the biomarker in said sample with reference concentrations or amounts of said biomarkers.

In embodiments of this sixth aspects the treatment for Alzheimer's disease may be selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof.

In other embodiments of the second to sixth aspects the sample is selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof. Preferably, the sample is CSF and/or the subject is a human subject, optionally a human subject previously diagnosed with mild cognitive impairment or a human
15 subject undergoing further clinical assessment of dementia.

In other embodiments of the second to sixth aspects the assaying in step a) and/or the measuring in step b) comprise:

i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or

20 ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or

iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the
25 biomarker panel; or

v) any combinations of i), ii), iii) and/or iv).

Preferably, the assaying step a) and/or the measuring step b) comprise detecting one or more fragments of said biomarker in the biomarker panel.

Optionally, the sample is immobilised on a solid support.

30 In a seventh aspect the present invention provides for a method for identifying biomarkers in a sample obtained from a subject, wherein the biomarkers are suitable for diagnosing or staging

Alzheimer's disease, wherein the method comprises using activate microglia cells (e.g. BV2 cells) and/or their culture media in mass spectrometry and/or wherein the biomarkers are identified in said sample by using activated microglia cells as a reference.

Preferably, the biomarker panel comprises the biomarkers as defined in the first aspect and its
5 embodiments.

In embodiments of this seventh aspect, the sample is selected from the group of CSF, blood, serum or plasma.

In an eighth aspect the present invention provides for a kit comprising reagents for assaying and/or measuring in a sample biomarkers of a biomarker panel according to the first aspect and
10 its embodiments.

In one embodiment of this eighth aspect, the reagents comprise one or more binding agents which specifically bind to the biomarkers of the biomarker panels. Preferably, the one or more binding agents are primary antibodies, wherein each primary antibody specifically binds to a different biomarkers of the biomarker panel.

15 In another embodiment, the reagents further comprise one or more secondary antibodies which specifically bind to said primary antibodies. Optionally, the secondary antibodies are labelled.

In other embodiments the sample is selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof.

Brief Description of the Drawings

20 **Figure 1.** Sequence of human phosphoglucomutase 1. Amino acids flagged by symbol □ or a * indicate amino acids which are replaced by a different or a modified amino acid in an isoform or a variant of human phosphoglucomutase 1, respectively.

Figure 2. Sequence of human thymosin beta-4. Amino acids outlined by a * indicates amino acids which are replaced by a different amino acid in a variant of human thymosin beta-4.

25 **Figure 3.** Up-regulation of peroxideroxin-1 (A), MARCKS-related protein (B), Meosin (C) and Actin (D) in AD CSF versus control CSF shown as function of the average signal intensity.

Figure 4. Up-regulation of Phosphoglucomutase-1 (A), Protein TMSB4XP4 (B), Ubiquitin carboxyl-terminal hydrolase isozyme L1 (C) and Vitamin-D binding protein (D) in AD CSF versus

control CSF shown as function of the average signal intensity.

Figure 5. Up-regulation of Dynactin Subunit 1 (A) and down-regulation of Cofilin-1 (B) in AD CSF versus control CSF shown as function of the average signal intensity.

Figure 6. Sample design showing the TMT¹⁰-plex set up used in experiment A (left panel) and
5 experiment B (right panel).

Definitions

The term “biomarker(s)” includes all biologically relevant forms of the protein identified, including post-translational modifications. For example, the biomarker can be present in a glycosylated, phosphorylated, multimeric, fragmented or precursor form. A biomarker fragment may be naturally
10 occurring or, for example, enzymatically generated and still retaining the biologically active function of the full protein. Fragments will typically be at least about 10 amino acids, usually at least about 50 amino acids in length, and can be as long as 300 amino acids in length or longer.

The term “canonical sequence” is used herein as to refer to the most prevalent sequence and/or the most similar sequence among orthologous species. In particular, unless otherwise specified,
15 the canonical sequence refers herein to the human sequence.

The term “KEGG pathway” refers to a collection of manually drawn pathway maps representing molecular interactions and reaction networks for metabolism, genetic information processing, environmental information processing, cellular processes, organismal systems, human diseases and drug development. “KEGG pathways mapping” is the process to map molecular datasets,
20 especially large-scale datasets in genomics, transcriptomics, proteomics, and metabolomics, to the KEGG pathway maps for biological interpretation of higher-level systemic functions; (<http://www.genome.jp/kegg/pathway.html>).

The term “concentration or amount” refers to the relative concentration or amount of biomarker in the sample, for example as determined by LC-MS/MS label free quantification approaches such
25 as area under the curve and spectral counting.

The term “comparing” or “compare” or grammatical equivalents thereof, means measuring the relative concentration or amount of a biomarker in a sample relative to other samples (for example protein concentrations or amounts stored in proprietary or public database).

The term “reference concentration or amount” or “reference value” refers to, but it is not limited to, protein concentrations or amounts stored in proprietary or public databases. The “reference concentration or amount” may have been obtained from a large screening of patients, or by reference to a known or previously determined correlation between such a determination and clinical information in control patients. For example, the reference values may be determined by comparison to the concentration or amount of the biomarkers in a control subject, for example a healthy person (i.e. without dementia) of similar age and gender as the subject. Alternatively, the reference values are values which can be found in literature such as the ApoE ϵ 4 allele presence whereby the presence or absence of the mutations at position 112 and 158 represent the reference to be compared to, or like the levels of total tau (T-tau) >350 ng/L, phospho-tau (P-tau) >80 ng/L and A β 42 <530 ng/L in the CSF (Hansson O, et al., Lancet Neurol. 2006, 5:228-34). In addition, the reference values may have been obtained from the same subject at one or more time points which precede in time the test time point. Such earlier sample may be taken one week or more, one month or more, three months or more, most preferably six months or more before the date of the test time point. In some embodiments, multiple earlier samples may be compared in a longitudinal manner and the slope of change in biomarker expression may be calculated as a correlate of cognitive decline. The reference value or reference level can be an absolute value; a relative value; a value that has an upper or a lower limit; a range of values; an average value; a median value, a mean value, or a value as compared to a particular control or baseline value.

According to the present invention, the level of a biomarker is increased when the level of said biomarker in a sample is higher than a reference value. The levels of a biomarker are considered to be higher than its reference value when it is at least 1.5%, at least 2%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%: at least 85%, at least 90%, at least 95%, at least 100%, at least 110%, at least 120%, at least 130%, at least 140%, at least 150% or more higher than the reference value.

Likewise, in the context of the present invention, the level of a biomarker is decreased when the level of said biomarker in a sample is lower than a reference value. The levels of a biomarker are considered to be lower than its reference value when it is at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%: at least 85%, at least 90%, at least 95%, at least 100%, at least 110%, at least 120%, at least 130%, at least 140%, at least 150% or more lower than the reference value.

The term "control" or as used herein "non AD control" or "non AD subject" refers to a tissue sample or a bodily fluid sample taken from a human or non-human subject diagnosed or presenting symptoms of a cognitive abnormality but defined, with respect to the existing biochemical tests, as non AD subjects.

- 5 The term "antibody" includes polyclonal antiserum, monoclonal antibodies, fragments of antibodies such as single chain and Fab fragments, and genetically engineered antibodies. The antibodies may be chimeric or of a single species.

The terms "selected reaction monitoring", "SRM" and "MRM" means a mass spectrometry assay whereby precursor ions of known mass-to-charge ratio representing known biomarkers are
10 preferentially targeted for analysis by tandem mass spectrometry in an ion trap or triple quadrupole mass spectrometer. During the analysis the parent ion is fragmented and the number of daughter ions of a second predefined mass-to-charge ratio is counted. Typically, an equivalent precursor ion bearing a predefined number of stable isotope substitutions but otherwise chemically identical to the target ion is included in the method to act as a quantitative internal
15 standard.

The term "isolated", or grammatical equivalents thereof, means throughout this specification, that the protein, antibody, polynucleotide or chemical molecule as the case may be, exists in a physical milieu distinct from that in which it may occur in nature.

As used herein, the term "subject" includes any human or non-human animal. The term
20 "non-human animal" includes all vertebrates, e.g., mammals and non-mammals, such as non-human primates, rodents, sheep, dogs, cats, horses, cows, chickens, amphibians, reptiles, etc.

The term "treat", "treating", "treatment", "prevent", "preventing" or "prevention", or grammatical equivalents thereof, includes therapeutic treatments, prophylactic treatments and applications in
25 which one reduces the risk that a subject will develop a disorder or other risk factor. Treatment does not require the complete curing of a disorder and encompasses the reduction of the symptoms or underlying risk factors.

The term "diagnosis", or grammatical equivalents thereof, as used herein, includes the provision of any information concerning the existence or presence, non-existence or absence or probability
30 of the disorder in a patient. It further includes the provision of information concerning the type or classification of the disorder or of symptoms which are or may be experienced in connection with

it. This may include, for example, diagnosis of the severity of the disorder. It encompasses prognosis of the medical course of the disorder, for example its duration, severity and the course of progression from mild cognitive impairment (MCI) to AD or other dementias.

5 The term “staging”, or grammatical equivalents thereof, as used herein, means identifying in a subject the stage of a neurocognitive disorder, in particular AD. For example, AD is characterised by 3 stage or 7 stages, depending on the diagnostic framework used. The Global Dementia Scale is one such measure of global function. It is measured by assessment of severity including cognition and function against a standardised set of severity criteria.

10 The term “efficacy” indicates the capacity for beneficial change of a given intervention (e.g. a drug, medical device, surgical procedure, etc.). If efficacy is established, that intervention is likely to be at least as good as other available interventions, to which it will have been compared. The term “efficacy” and “effectiveness” are used herein interchangeably.

The term “comprising” indicates that the subject includes all the elements listed, but may, optionally, also include additional, unnamed elements (i.e. open).

15 The term “and/or” where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. For example “A and/or B” is to be taken as specific disclosure of each of (i) A, (ii) B and (iii) A and B, just as if each is set out individually herein.

20 Unless the context dictates otherwise, the definitions of the features/terms set out above are not limited to any particular aspect or embodiment of the invention and apply equally to all aspects and embodiments which are described herein.

Abbreviations

25 CSF (cerebrospinal fluid); LBD (Lewy body dementia); FTD (fronto-temporal dementia); VaD (vascular dementia); ALS (amyotrophic lateral sclerosis); CJD (Creutzfeldt-Jakob disease); CNS (central nervous system); LPS (lipopolysaccharide); INF γ (interferon-gamma); TMT $\text{\textcircled{R}}$ (Tandem Mass Tag $\text{\textcircled{R}}$); TEAB (Tetra-ethylamonium Bicarbonate), SDS (Sodium dodecyl sulfate); TCEP (Tris(2-carboxyethyl)phosphine); ACN (Acetonitril); PGM1 (phosphoglucomutase 1); TMS4 (Thymosin beta-4).

Detailed Description

The brains of patients with AD are characterized by amyloid plaques and neurofibrillary “tangles”. Numerous lines of genetic, epidemiologic, and pathologic evidence point to the amyloid precursor protein and its proteolytic product, amyloid β -peptide ($A\beta$), as central players in AD etiology (Selkoe DJ, *Physiol. Rev.* 2001, 81:741-66). While plaques and tangles are most often associated
 5 with the disease, a third pathological feature “gliosis” or inflammation of the brain is also much more integral to AD patho-etiology than once appreciated.

Early events in neurodegenerative pathology, including those typical of AD, involves activation of microglial cells (Mandrekar S et al., *CNS Neurol Disord Drug Targets.* 2010, 9:156-67). Much interest has been focused on the role of microglia in neurodegenerative diseases in recent times
 10 due to an increasing number of genetic and biomarker discovery programs and growing evidence suggesting that inflammation has a role in disease pathogenesis (Wisniewski HM, et al., *Acta Neuropathol.* 1992, 84:117-27).

Microglia are a type of glial cell and are the resident macrophage-like cells of the central nervous system (CNS) (Mandrekar S et al., *CNS Neurol Disord Drug Targets.* 2010, 9:156-67). Within the
 15 CNS, microglial cells perform a variety of different functions related to the immune response and the maintenance of cellular homeostasis. Microglia sense the environment around them, can be activated by various factors and referee neuroinflammatory and neuroprotective responses in the brain, responding to the formation of amyloid plaques in brains of AD patients. This activation can take different forms, and the so called M1 activation state causes the release of pro-inflammatory
 20 cytokines such as $TNF-\alpha$, $IL-1\beta$ and reactive oxygen/nitrogen species ROS/NOS (Henkel J, *Neuroimmune Pharmacol.* 2009, 4:389-98). This ultimately may cause or increase neuronal damage.

There appears to be different mechanisms of microglial activation, including in vivo intrinsic regulation, $A\beta$ phagocytosis, and microglial $A\beta$ receptor complex (Mandrekar S et al., *CNS Neurol*
 25 *Disord Drug Targets.* 2010, 9:156-67).

The present inventors hypothesize that, during the early stage of AD pathology, activated microglia will secrete distinct proteins into the brain. Such proteins would then transfer into the cerebrospinal fluid (CSF) and other biological fluids and could be identified and validated as biomarkers for early AD pathology.

30 1. Biomarker panels and methods of using thereof

The present invention relates to such novel biomarkers and their use in methods for diagnosing,

staging and assessing the likelihood of developing a neurocognitive disorder, in particular Alzheimer's disease (AD).

The biomarker panels disclosed herein represent a peripheral signal that reflects events and pathways modulation in brain tissue that could not be tested by biopsy or other invasive tests.

- 5 Because the biomarker panels reflect the neuroinflammation resulting from microglia activation in AD subject, they represent ideal measurable indicators of the disease at an early stage.

The biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2.

- 10 Human phosphoglucomutase 1 (PMG1; P36871) is an isozyme of phosphoglucomutase (PGM) and belongs to the phosphohexose mutase family. There are several PGM isozymes, which are encoded by different genes and catalyse the transfer of phosphate between the 1 and 6 positions of glucose. Mutations in this gene cause glycogen storage disease type 14. Alternatively spliced transcript variants encoding different isoforms have been identified.

- 15 Human thymosin beta-4 (TMSB4X; P62328) plays an important role in the organization of the cytoskeleton. It binds to and sequesters actin monomers (G-actin) and therefore inhibits actin polymerization.

- The biomarker panel may also comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 and thymosin beta-4 comprising or having the amino acid
20 sequence of SEQ ID NO:2.

The biomarker panel may also comprise an isoform or a variant or a fragment of phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1; and/or a variant or a fragment of thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2.

- 25 An isoform is described herein as an alternative protein sequence with respect to the canonical sequence. Isoforms can be generated from the same gene by a single or by the combination of alternative promoter usage, alternative splicing, alternative initiation and ribosomal frameshifting.

- A variant is described herein as to include natural variants such as (naturally occurring) polymorphisms, variations between strains, isolates or cultivars, disease-associated mutations
30 and RNA editing events. A variant is generally reported as the amino acid change with respect to

the canonical sequence. Most naturally occurring polymorphisms (also called single amino acid polymorphisms or SAPs) are due to a single nucleotide change at the codon level. RNA editing events include conversion, insertion and deletion of nucleotides.

5 A fragment is described herein as the result of proteolytic (enzymatic or else) cleavage of a protein. Fragments may be the results of natural proteolytic cleavage for example fragments generated during the activation of complement, the clotting cascade, or from enzymatic cleavage of matrix proteins. Alternatively, fragments may be generated *in-vivo* and/or *in-vitro* for example with proteases.

10 In one embodiment, the variant of phosphoglucomutase 1 comprises or has the amino acid sequence of SEQ ID NO: 1 and wherein

- a) threonine at position 19 is replaced by alanine; or
- b) asparagine at position 38 is replaced by tyrosine; or
- c) glutamine at position 41 is replaced by arginine; or
- d) aspartic acid at position 62 is replaced by histamine; or
- 15 e) lysine at position 68 is replaced by methionine; or
- f) isoleucine at position 88 is replaced by valine; or
- g) threonine at position 115 is replaced by alanine; or
- h) glycine at position 121 is replaced by arginine; or
- i) arginine at position 221 is replaced by cysteine; or
- 20 j) aspartic acid at position 263 is replaced by glycine or tyrosine; or
- k) glycine at position 291 is replaced by arginine; or
- l) glycine at position 330 is replaced by arginine; or
- m) glutamic acid at position 377 is replaced by lysine; or
- n) glutamic acid at position 388 is replaced by lysine; or
- 25 o) tyrosine at position 420 is replaced by histidine; or
- p) valine at position 501 is replaced by isoleucine; or
- q) leucine at position 516 is replaced by proline; or
- r) methionine at position 1 is N-acetylmethionine; or
- s) lysine at position 16 is N6-acetyllysine; or
- 30 t) serine at position 117 is phosphoserine; or
- u) lysine at position 349 is N6-acetyllysine; or
- v) tyrosine at position 353 is phosphotyrosine; or
- w) lysine at position 419 is N6-succinyllysine; or
- x) threonine at position 467 is phosphothreonine; or

y) threonine at position 507 is phosphothreonine.

Figure 1 shows the human sequence of human phosphoglucomutase 1 (SEQ ID NO:1); flagged by symbol □ are those amino acids that are replaced with a different amino acid in isoforms of human phosphoglucomutase 1 as indicated above in a) to q). Amino acids flagged by a * are those amino acids which are replaced by modified amino acids in isoforms of human phosphoglucomutase 1 as indicated above in r) to y).

In another embodiment the isoform of phosphoglucomutase 1 comprises or has the amino acid sequence of

- a) SEQ ID NO:3 (isoform 2) and wherein methionine 1 is N-acetylmethionine; or
- 10 b) SEQ ID NO:1 from amino acids 198 to 562 (isoform 3).

In another embodiment the fragment of phosphoglucomutase 1 comprises or has the amino acid sequence of any one of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, or SEQ ID NO: 10; or SEQ ID NO: 11; or SEQ ID NO: 12 ; or SEQ ID NO: 13.

In another embodiment the variant of thymosin beta-4 comprises or has the amino acid sequence of SEQ ID NO: 2 and

- a) lysine at position 12 is replaced by proline; or
- b) serine at position 16 replaced by alanine; or
- c) leucine at position 18 is replaced by alanine or proline; or
- d) serine at position 2 is N-acetylserine; or
- 20 e) lysine at position 26 is N6-acetyllysine; or
- f) lysine at position 9 is N6-acetyllysine.

Figure 2 shows the sequence human of thymosin beta-4 (SEQ ID NO:2); flagged by symbol □ are those amino acids that are replaced with a different amino acid in isoforms of human thymosin beta-4 as indicated in a) to c) in the previous paragraph. Amino acids flagged by a * are those amino acids which are replaced by modified amino acids in isoforms of human thymosin beta-4 as indicated above in d) to f) in the previous paragraph.

In another embodiment the fragment of thymosin beta-4 comprises or has the amino acid sequence of any one of SEQ ID NO: 14, SEQ ID NO: 15, or SEQ ID NO: 16.

As shown later herein in the experimental section, the biomarker panels disclosed herein have been identified as a set of upregulated proteins found in the CSF of AD patients with respect to

individual who present mild cognitive impairment but are not diagnosed with AD. In general clinical practice, biomarkers are measured as a set of at least 2, preferably at least 3 or 4.

Therefore, the biomarker panel according to the invention may further comprise ubiquitin carboxy-terminal hydrolase L1 (UCH-L1; D6R956) which comprises or has an amino acid
 5 sequence of SEQ ID NO:4 or an isoform or a variant or a fragment thereof; and/or vitamin D binding protein (VBPD; D6RBJ7) which comprises or has an amino acid sequence of SEQ ID NO: 5 or an isoform or a variant or a fragment thereof.

Examples of isoforms, variants or fragments of ubiquitin carboxy-terminal hydrolase L1 or vitamin D binding protein can be found in publically accessible databases such as Uniprot.

10 In one embodiment, the fragment of ubiquitin carboxy-terminal hydrolase L1 has or comprises the sequence as shown in SEQ ID NO:17. In another embodiment, the fragment of vitamin D binding protein has or comprises the sequence as shown in SEQ ID NO:18.

Hence, in one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof;
 15 and thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and ubiquitin carboxy-terminal hydrolase L1 comprising or having the amino acid sequence of SEQ ID NO:4 or an isoform or a variant or a fragment thereof and/or vitamin D binding protein comprising or having the amino acid sequence of SEQ ID NO: 5 or an isoform or variant or a fragment thereof.

20 The biomarker panel may further comprise one or more biomarkers selected from proteins involved in a KEGG pathway wherein the KEGG pathway is selected from the group of complement and coagulation cascade, or glycolysis/glycogenesis, or prion disease, or amino and nucleotide sugar metabolism, or antigen processing and presentation, or extracellular matrix-receptor interaction, or focal adhesion, or regulation of actin cytoskeleton or
 25 alanine/aspartate/glutamate metabolism.

The biomarker panel may further comprise at least one, optionally two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
 30 thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a

fragment thereof; and at least one, optionally two or more biomarkers selected from Table 1 or fragments thereof.

TABLE 1

<u>Uniprot ID</u>	<u>Protein Name</u>	<u>All Uniprot matches</u>
K7EJ74	116 kDa U5 small nuclear ribonucleoprotein component	K7EJ74;Q15029-3;K7EP67;Q15029;Q15029-2
B4DJF2	14-3-3 protein epsilon (cDNA FLJ51975, moderately similar to 14-3-3 protein epsilon (14-3-3E))	B4DJF2;I3L3T1;P62258
E5RH77	40S ribosomal protein S14	E5RH77;H0YB22;P62263
M0R210	40S ribosomal protein S16 (Ribosomal protein S16, isoform CRA_a)	M0R210;P62249
P63220	40S ribosomal protein S21	P63220;Q8WVC2
D6R9B6	40S ribosomal protein S3a (Ribosomal protein S3A, isoform CRA_e)	D6R9B6;D6RAT0;D6RG13;E9PFI5;F5H4F9;H0Y9Y4;P61247;D6RB09
B5MCP9	40S ribosomal protein S7	B5MCP9;P62081
P10809	60 kDa heat shock protein, mitochondrial (60 kDa chaperonin) (Chaperonin 60) (CPN60) (Heat shock protein 60) (HSP-60) (Hsp60) (HuCHA60) (Mitochondrial matrix protein P1) (P60 lymphocyte protein)	E7ESH4;E7EXB4;P10809
P30050	60S ribosomal protein L12	P30050;P30050-2
H0YKD8	60S ribosomal protein L28	H0YKD8;H0YLP6;H0YMF4;P46779;P46779-2;P46779-3;P46779-4;P46779-5
C9K025	60S ribosomal protein L35a	C9K025;F8WB72;F8WBS5;P18077
P11021	78 kDa glucose-regulated protein (GRP-78) (Endoplasmic reticulum lumenal Ca(2+)-binding protein grp78) (Heat shock 70 kDa protein 5) (Immunoglobulin heavy chain-binding protein) (BiP)	P11021
A6NL76	Actin, alpha skeletal muscle	A6NL76;B8ZZJ2;C9JTX5;C9JUM1;F6QUT6;F8WB63;G5E9R0;I3L1U9;I3L3R2;J3KT65;K7EM38;P60709;P62736;P63261;P63267;P68032;P68133;Q562R1;Q5T8M7;Q5T8M8;C9JFL5;C9JZR7;E7EVS6
P01009	Alpha-1-antitrypsin (Alpha-1 protease inhibitor) (Alpha-1-antiproteinase) (Serpine A1) [Cleaved into: Short peptide from AAT (SPAAT)]	P01009;P01009-2
P02765	Alpha-2-HS-glycoprotein (Alpha-2-Z-globulin) (Ba-alpha-2-glycoprotein) (Fetuin-A) [Cleaved into: Alpha-2-HS-glycoprotein chain A; Alpha-2-HS-glycoprotein chain B]	P02765
F5GXS2	Alpha-actinin-4	F5GXS2;H0YJ11;H0YJW3;H7C144;H7C5W8;H9KV75;O43707;O43707-2;O43707-3;P12814;P12814-2;P12814-3;P12814-4
P06733	Alpha-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hydro-lyase) (C-myc promoter-binding protein) (Enolase)	P06733;P06733-2

	1) (MBP-1) (MPB-1) (Non-neural enolase) (NNE) (Phosphopyruvate hydratase) (Plasminogen-binding protein)	
J3KMX3	Alpha-fetoprotein	J3KMX3;P02771
E9PEV0	Amyloid beta A4 protein*	E9PEV0;P05067;P05067-11;P05067-2;P05067-3;P05067-4;P05067-5;P05067-6;P05067-7;P05067-8;P05067-9
E9PK76	Amyloid-like protein 2	E9PK76;E9PQS3;Q06481;Q06481-2;Q06481-3;Q06481-4;Q06481-5;Q06481-6;E9PSC7
D6RBE9	Annexin	D6RBE9;D6RBL5;P08758
A8MUN2	Apolipoprotein B-100	A8MUN2;P04114
P00505	Aspartate aminotransferase, mitochondrial (mAspAT) (EC 2.6.1.1) (EC 2.6.1.7) (Fatty acid-binding protein) (FABP-1) (Glutamate oxaloacetate transaminase 2) (Kynurenine aminotransferase 4) (Kynurenine aminotransferase IV) (Kynurenine--oxoglutarate transaminase 4) (Kynurenine--oxoglutarate transaminase IV) (Plasma membrane-associated fatty acid-binding protein) (FABPpm) (Transaminase A)	P00505-2;P00505
Q9NVP1	ATP-dependent RNA helicase DDX18 (EC 3.6.4.13) (DEAD box protein 18) (Myc-regulated DEAD box protein) (MrDb)	Q9NVP1
O75531	Barrier-to-autointegration factor (Breakpoint cluster region protein 1) [Cleaved into: Barrier-to-autointegration factor, N-terminally processed]	O75531
F5H6I0	Beta-2-microglobulin form pl 5.3	F5H6I0;H0YLF3;P61769
P80723	Brain acid soluble protein 1 (22 kDa neuronal tissue-enriched acidic protein) (Neuronal axonal membrane protein NAP-22)	P80723;P80723-2;U3KQP0
P04003	C4b-binding protein alpha chain (C4bp) (Proline-rich protein) (PRP)	P04003
F8VPD4	CAD protein	F8VPD4;H7C2E4;P27708
E7EMB3	Calmodulin	E7EMB3;E7ETZ0;H0Y7A7;P62158;G3V361;Q96HY3
P04040	Catalase (EC 1.11.1.6)	P04040
B4DRT0	cDNA FLJ50184, highly similar to Histone-binding protein RBBP4	B4DRT0;E9PC52;H0YCT5;H0YDK2;H0YEU5;H0YF10;Q09028;Q09028-2;Q09028-3;Q09028-4;Q16576;Q16576-2;Q5JP02
B4DY72	cDNA FLJ52360, highly similar to Heat-shock protein 105 kDa	B4DY72;Q92598-4;Q92598;Q92598-2;Q92598-3
B4E3Q1	cDNA FLJ61580, highly similar to Calsyntenin-1	B4E3Q1;O94985;O94985-2;Q5SR54
P62633	Cellular nucleic acid-binding protein (CNBP) (Zinc finger protein 9)	P62633-7;P62633;P62633-2;P62633-3;P62633-4;P62633-5;P62633-6;P62633-8
Q9Y696	Chloride intracellular channel protein 4 (Intracellular chloride ion channel protein p64H1)	Q9Y696
P12259	Coagulation factor V (Activated protein C	P12259

	cofactor) (Proaccelerin, labile factor) [Cleaved into: Coagulation factor V heavy chain; Coagulation factor V light chain]	
E9PGP2	Coagulation factor XI	E9PGP2;P03951;P03951-2;X6R3B1
J3KR35	Coiled-coil domain containing 12, isoform CRA_a (Coiled-coil domain-containing protein 12)	J3KR35;Q8WUD4
P01031	Complement C5 (C3 and PZP-like alpha-2-macroglobulin domain-containing protein 4) [Cleaved into: Complement C5 beta chain; Complement C5 alpha chain; C5a anaphylatoxin; Complement C5 alpha' chain]	P01031
P10643	Complement component C7	P10643
F5GX68	Cytosine-specific methyltransferase (EC 2.1.1.37)	F5GX68;P26358;P26358-2;P26358-3
E5RIA2	Ectonucleotide pyrophosphatase/phosphodiesterase family member 2	E5RIA2;E7EUF1;Q13822;Q13822-2;Q13822-3
Q9H4M9	EH domain-containing protein 1 (PAST homolog 1) (hPAST1) (Testilin)	Q9H4M9;Q9NZN3
A6PW80	Elongation factor 1-alpha 1	P68104;Q05639;Q5JR01;Q5VTE0;A6PW80
K7EM90	Enolase (EC 4.2.1.11)	K7EM90;P06733;P06733-2
P47813	Eukaryotic translation initiation factor 1A, X-chromosomal (eIF-1A X isoform) (Eukaryotic translation initiation factor 4C) (eIF-4C)	P47813;X6RAC9
C9JQN7	Eukaryotic translation initiation factor 3 subunit B	C9JQN7;P55884;P55884-2
O60841	Eukaryotic translation initiation factor 5B (eIF-5B) (Translation initiation factor IF-2)	O60841
Q15024	Exosome complex component RRP42 (Exosome component 7) (Ribosomal RNA-processing protein 42) (p8)	Q15024
O14980	Exportin-1 (Exp1) (Chromosome region maintenance 1 protein homolog)	O14980
B1AK85	F-actin-capping protein subunit beta (cDNA FLJ43095 fis, clone CORDB2000541, highly similar to F-actin capping protein subunit beta)	B1AK85;B1AK87;B1AK88;F6Q0E3;F6USW4;P47756;P47756-2
P02671	Fibrinogen alpha chain [Cleaved into: Fibrinopeptide A; Fibrinogen alpha chain]	P02671;P02671-2
C9JC84	Fibrinogen gamma chain	C9JC84;C9JEU5;P02679;P02679-2
E9PHF0	Filamin-A	E9PHF0;P21333;P21333-2;Q5HY54
F8WE98	Filamin-A	F8WE98;O75369;O75369-2;O75369-3;O75369-4;O75369-5;O75369-6;O75369-8;O75369-9;P21333;P21333-2;Q14315;Q14315-2;Q5HY54
E7EN95	Filamin-B	E7EN95;O75369;O75369-2;O75369-3;O75369-4;O75369-5;O75369-6;O75369-7;O75369-8;O75369-9
H3BPS8	Fructose-bisphosphate aldolase A	H3BPS8;H3BQN4;H3BR04;H3BU78;J3KPS3;P04075;P04075-2
H3BMQ	Fructose-bisphosphate aldolase A	H3BMQ8;H3BQN4;H3BR04;H3BUH7;J3KPS3;P

8		04075
P17931	Galectin-3 (Gal-3) (35 kDa lectin) (Carbohydrate-binding protein 35) (CBP 35) (Galactose-specific lectin 3) (Galactoside-binding protein) (GALBP) (IgE-binding protein) (L-31) (Laminin-binding protein) (Lectin L-29) (Mac-2 antigen)	P17931
P06396	Gelsolin (AGEL) (Actin-depolymerizing factor) (ADF) (Brevin)	P06396
E7EUT5	Glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12)	E7EUT5;P04406;P04406-2
B5MDF5	GTP-binding nuclear protein Ran (RAN, member RAS oncogene family, isoform CRA_c)	B5MDF5;H0YFC6;J3KQE5;P62826
H0Y300	Haptoglobin	H0Y300;H3BS21;J3QLC9;J3QR68;P00738;P00739;P00739-2;P00738-2
G3V1N2	HCG1745306, isoform CRA_a (Hemoglobin subunit alpha)	G3V1N2;P69905
A8K7Q2	Heat shock cognate 71 kDa protein (cDNA FLJ77848)	A8K7Q2;E7EP94;E9PKE3;E9PNE6;E9PS65;P08107;P08107-2;P11142;P17066;P34931;P54652;V9GZ37;E9PM13
P08238	Heat shock protein HSP 90-beta (HSP 90) (Heat shock 84 kDa) (HSP 84) (HSP84)	P08238
E9PEW8	Hemoglobin subunit delta	E9PEW8;E9PFT6;F8W6P5;P02042;P68871
F8VTQ5	Heterogeneous nuclear ribonucleoprotein A1	F8VTQ5;F8VYN5;F8VZ49;F8W6I7;P09651;P09651-2;P09651-3;Q32P51
Q00839	Heterogeneous nuclear ribonucleoprotein U (hnRNP U) (Scaffold attachment factor A) (SAF-A) (p120) (pp120)	Q00839;Q00839-2;Q5RI18
P22626	Heterogeneous nuclear ribonucleoproteins A2/B1 (hnRNP A2/B1)	P22626;P22626-2
C9J0D1	Histone H2A	C9J0D1;C9J386;P0C0S5;Q71UI9;Q71UI9-2;Q71UI9-3;Q71UI9-4
Q8N257	Histone H2B type 3-B (H2B type 12)	Q8N257;Q96A08;Q99880
P01871	Ig mu chain C region	P01871;P01871-2;P04220
Q9Y6R7	IgG Fc-binding protein (Fc gamma-binding protein antigen) (Fc gamma BP)	Q9Y6R7
Q15181	Inorganic pyrophosphatase (EC 3.6.1.1) (Pyrophosphate phospho-hydrolase) (PPase)	Q15181;Q5SQT6
Q16270	Insulin-like growth factor-binding protein 7 (IBP-7) (IGF-binding protein 7) (IGFBP-7) (IGFBP-rP1) (MAC25 protein) (PGI2-stimulating factor) (Prostacyclin-stimulating factor) (Tumor-derived adhesion factor) (TAF)	Q16270;Q16270-2
F5H7E1	Inter-alpha-trypsin inhibitor heavy chain H1*	F5H7E1;F8WAS2;P19827
E7ET33	Inter-alpha-trypsin inhibitor heavy chain H3	E7ET33;Q06033;Q06033-2
O75874	Isocitrate dehydrogenase [NADP] cytoplasmic (IDH) (EC 1.1.1.42) (Cytosolic NADP-isocitrate dehydrogenase) (IDP) (NADP(+)-specific ICDH) (Oxalosuccinate decarboxylase)	O75874

Q9BR39	Junctophilin-2 (JP-2) (Junctophilin type 2)	Q9BR39;Q9BR39-2
P13645	Keratin, type I cytoskeletal 10 (Cytokeratin-10) (CK-10) (Keratin-10) (K10)	P13645;Q7Z3Y7
K7EMD9	Keratin, type I cytoskeletal 13	K7EMD9;K7ERE3;P13645;P13646;P13646-2;P13646-3;Q2M2I5
P02533	Keratin, type I cytoskeletal 14 (Cytokeratin-14) (CK-14) (Keratin-14) (K14)	P02533;P08779;P13645;Q7Z3Y7;Q7Z3Y8;Q7Z3Y9;Q7Z3Z0
A8MT21	Keratin, type I cytoskeletal 15	A8MT21;B3KRA2;C9JM50;C9JTG5;F5GWP8;K7EMS3;K7EPJ9;P02533;P08727;P08779;P19012;Q04695
K7EQQ3	Keratin, type I cytoskeletal 9	K7EQQ3;P35527
P04264	Keratin, type II cytoskeletal 1 (67 kDa cytokeratin) (Cytokeratin-1) (CK-1) (Hair alpha protein) (Keratin-1) (K1) (Type-II keratin Kb1)	P04264
F5GY66	Keratin, type II cytoskeletal 1b*	F5GY66;Q7Z794
P35908	Keratin, type II cytoskeletal 2 epidermal (Cytokeratin-2e) (CK-2e) (Epithelial keratin-2e) (Keratin-2 epidermis) (Keratin-2e) (K2e) (Type-II keratin Kb2)	P35908
P04259	Keratin, type II cytoskeletal 6B (Cytokeratin-6B) (CK-6B) (Keratin-6B) (K6B) (Type-II keratin Kb10)	P04259;P04264
P01042	Kininogen-1 (Alpha-2-thiol proteinase inhibitor) (Fitzgerald factor) (High molecular weight kininogen) (HMWK) (Williams-Fitzgerald-Flaujeac factor) [Cleaved into: Kininogen-1 heavy chain; T-kinin (Ile-Ser-Bradykinin); Bradykinin (Kallidin I); Lysyl-bradykinin (Kallidin II); Kininogen-1 light chain; Low molecular weight growth-promoting factor]	P01042;P01042-2;P01042-3
E7EQB2	Lactotransferrin	E7EQB2;E7ER44;P02788;P02788-2
P49006	MARCKS-related protein (MARCKS-like protein 1) (Macrophage myristoylated alanine-rich C kinase substrate) (Mac-MARCKS) (MacMARCKS)	P49006
Q9NU22	Midasin (MIDAS-containing protein)	Q9NU22
P26038	Moesin (Membrane-organizing extension spike protein)	P26038
C9JH43	Neuronal cell adhesion molecule	C9JH43;C9JYY6;F8W775;Q92823;Q92823-2;Q92823-3;Q92823-4;Q92823-5;Q92823-6
O15240	Neurosecretory protein VGF [Cleaved into: Neuroendocrine regulatory peptide-1 (NERP-1); Neuroendocrine regulatory peptide-2 (NERP-2); Antimicrobial peptide VGF[554-577]]	O15240
C9IZL7	Non-POU domain-containing octamer-binding protein	C9IZL7;C9J4X2;Q15233;Q15233-2;Q8WXF1;Q8WXF1-2;C9JYS8;X6RDA4
P23515	Oligodendrocyte-myelin glycoprotein	P23515
C9J5S7	Peptidyl-prolyl cis-trans isomerase (EC 5.2.1.8)	C9J5S7;F8WE65;P62937

P62937	Peptidyl-prolyl cis-trans isomerase A (PPlase A) (EC 5.2.1.8) (Cyclophilin A) (Cyclosporin A-binding protein) (Rotamase A) [Cleaved into: Peptidyl-prolyl cis-trans isomerase A, N-terminally processed]	P62937;Q567Q0
P23284	Peptidyl-prolyl cis-trans isomerase B (PPlase B) (EC 5.2.1.8) (CYP-S1) (Cyclophilin B) (Rotamase B) (S-cyclophilin) (SCYLP)	P23284
Q9Y3C6	Peptidyl-prolyl cis-trans isomerase-like 1 (PPlase) (EC 5.2.1.8) (Rotamase PPIL1)	Q9Y3C6
Q06830	Peroxiredoxin-1 (EC 1.11.1.15) (Natural killer cell-enhancing factor A) (NKEF-A) (Proliferation-associated gene protein) (PAG) (Thioredoxin peroxidase 2) (Thioredoxin-dependent peroxide reductase 2)	Q06830
H7C3T4	Peroxiredoxin-4	H7C3T4;Q13162
B7Z7A9	Phosphoglycerate kinase 1 (EC:2.7.2.3) (Cell migration-inducing gene 10 protein) (Primer recognition protein 2) (prp 2)	B7Z7A9;E7ERH5;P00558;P07205
P18669	Phosphoglycerate mutase 1 (EC 3.1.3.13) (EC 5.4.2.11) (EC 5.4.2.4) (BPG-dependent PGAM 1) (Phosphoglycerate mutase isozyme B) (PGAM-B)	P18669;P36871;P36871-2;P36871-3
H0YGH6	Pregnancy zone protein*	H0YGH6;P01023;P20742;P20742-2
P12004	Proliferating cell nuclear antigen (PCNA) (Cyclin)	P12004
H0YKK6	Proteasome activator complex subunit 1	H0YKK6;Q06323-3;Q06323;Q06323-2
F5H246	Protein NAMPTL	F5H246;P43490;Q5SYT8
Q15437	Protein transport protein Sec23B (SEC23-related protein B)	Q15437;Q5QPE1
A6NEC2	Puromycin-sensitive aminopeptidase-like protein (EC 3.4.11.-)	A6NEC2;A6NEC2-2;B7Z463;E5RJ24;I3L083;E9PLK3;F5GZY4;H0YAQ6;P55786;E7EWZ2
H0Y825	Putative homeodomain transcription factor 1	H0Y825;Q5TCQ3;Q5TCQ5;Q9UMS5;Q9UMS5-2
A6NM43	Putative T-complex protein 1 subunit theta-like 1	A6NM43;Q96SF2
H3BQ34	Pyruvate kinase PKM (EC 2.7.1.40) (Cytosolic thyroid hormone-binding protein) (CTHBP) (Opa-interacting protein 3) (OIP-3) (Pyruvate kinase 2/3) (Pyruvate kinase muscle isozyme) (Thyroid hormone-binding protein 1) (THBP1) (Tumor M2-PK) (p58)	H3BQ34;H3BT25;H3BTJ2;H3BTN5;H3BUW1;P14618;P14618-2;P14618-3
A8MSP2	RAB37, member RAS oncogene family, isoform CRA_e (Ras-related protein Rab-37) (cDNA FLJ45130 fis, clone BRAWH3037428, highly similar to Homo sapiens RAB37, member RAS oncogene family (RAB37), transcript variant 3, mRNA)	Q9H082;G3V196;G3V562;J3QSF4;P59190;P59190-2;Q6MZX6;Q9NRW1-2;C9JB90;C9JU14;H0YGL6;H7BYW1;J3KR73;P20340;P20340-2;P20340-4;Q14964;Q9NRW1;A8MSP2;A8MTC6;A8MZI4;B4DEK7;B7Z3L0;C9JFM7;Q86YS6-2;E9P1I8;E9PJQ5;E9PMJ1;E9PNB9;E9PRF7;E9PS06;F5GY21;F5H157;H0YDK7;H0YMN7;H0YNE9;M0R0X1;M0R1E0;M0R257;O95716;P20336;P20337;P20338;P61006;P61018;P61018-2;P61026;P61106;P62820;Q15286;Q15286-2;Q15771;Q6IQ22;Q15771-2;Q6PIK3;Q86YS6;Q92928;Q92

		930;Q96AX2;Q96AX2-2;Q96AX2-3;Q96AX2-4;Q96DA2;Q96E17;Q9H0U4;X6RFL8
P60602	Reactive oxygen species modulator 1 (ROS modulator 1) (Epididymis tissue protein Li 175) (Glyrichin) (Mitochondrial targeting GxxxG motif protein) (MTGM) (Protein MGR2 homolog)	P60602
A8MT72	Reticulon	B7Z4M1;F5H617;O95197;O95197-2;O95197-3;O95197-4;O95197-5;O95197-6;O95197-7;A8MT72;Q16799;Q16799-2;Q16799-3
P02753	Retinol-binding protein 4 (Plasma retinol-binding protein) (PRBP) (RBP) [Cleaved into: Plasma retinol-binding protein(1-182); Plasma retinol-binding protein(1-181); Plasma retinol-binding protein(1-179); Plasma retinol-binding protein(1-176)]	P02753;Q5VY30
G3V357	Ribonuclease pancreatic	G3V357;P07998
B3KQV6	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform (cDNA FLJ33169 fis, clone ADRGL2000384, highly similar to Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform)	B3KQV6;E9PH38;F5H3X9;P30153
P35542	Serum amyloid A-4 protein (Constitutively expressed serum amyloid A protein) (C-SAA)	P35542
J3KPM9	Signal transducer and activator of transcription	J3KPM9;P42224;P42224-2
H3BQ21	Signal-regulatory protein beta-1 isoform 3	H3BQ21;H3BSK5;H3BU43;P78324;P78324-2;P78324-4;Q5TFQ8
Q9H2G2	STE20-like serine/threonine-protein kinase (STE20-like kinase) (hSLK) (EC 2.7.11.1) (CTCL tumor antigen se20-9) (STE20-related serine/threonine-protein kinase) (STE20-related kinase) (Serine/threonine-protein kinase 2)	Q9H2G2;Q9H2G2-2
P04179	Superoxide dismutase [Mn], mitochondrial (EC 1.15.1.1)	P04179;P04179-2;P04179-4
P07996	Thrombospondin-1	P07996;P07996-2
P62328	Thymosin beta-4 (T beta-4) (Fx) [Cleaved into: Hematopoietic system regulatory peptide (Seraspenide)]	P62328;Q5T4B6
Q13263	Transcription intermediary factor 1-beta (TIF1-beta) (E3 SUMO-protein ligase TRIM28) (EC 6.3.2.-) (KRAB-associated protein 1) (KAP-1) (KRAB-interacting protein 1) (KRIP-1) (Nuclear corepressor KAP-1) (RING finger protein 96) (Tripartite motif-containing protein 28)	Q13263;Q13263-2
P02766	Transthyretin (ATTR) (Prealbumin) (TBPA)	P02766
P60174	Triosephosphate isomerase (TIM) (EC 5.3.1.1) (Triose-phosphate isomerase)	P60174;P60174-1
Q08J23	tRNA (cytosine(34)-C(5))-methyltransferase (EC 2.1.1.203) (Myc-induced SUN domain-containing protein) (Misu)	Q08J23;Q5SWD1

	(NOL1/NOP2/Sun domain family member 2) (Substrate of AIM1/Aurora kinase B) (tRNA (cytosine-5-)-methyltransferase) (tRNA methyltransferase 4 homolog) (hTrm4)	
G5EA42	Tropomodulin 2 (Neuronal), isoform CRA_a (Tropomodulin-2)	G5EA42;H0YMA2;Q9NZR1;Q9NZR1-2
F8W696	Truncated apolipoprotein A-I	F8W696;P02647
C9J2C0	Tubulin alpha-8 chain	F5H5D3;F8VQQ4;P68363;Q13748;Q13748-2;Q 6PEY2;Q71U36;Q71U36-2;Q9BQE3;F8VVB9;P 68366-2;C9J2C0;C9JDS9;P68366;Q9NY65;Q9 NY65-2
P43403	Tyrosine-protein kinase ZAP-70 (EC 2.7.10.2) (70 kDa zeta-chain associated protein) (Syk-related tyrosine kinase)	P43403;P43403-2;P43403-3;P43405;P43405-2; Q8NFD2
F5GY79	Tyrosine-protein phosphatase non-receptor type 6	F5GY79;F5H0N8;F5H5H9;P29350;P29350-2;P2 9350-3;P29350-4;F5H1Z8
D6R956	Ubiquitin carboxyl-terminal hydrolase isozyme L1	D6R956;D6R974;D6RE83;P09936
P62979	Ubiquitin-40S ribosomal protein S27a (Ubiquitin carboxyl extension protein 80) [Cleaved into: Ubiquitin; 40S ribosomal protein S27a]	P62979
F5H4L7	Vacuolar protein sorting-associated protein 26A*	F5H4L7;G3V1N8;O75436;O75436-2;S4R3Q6
B0YJC4	Vimentin (Vimentin variant 3)	B0YJC4;P08670;P17661
D6RBJ7	Vitamin D-binding protein	D6RBJ7;D6RF20;D6RF35;P02774;P02774-3
B5MCX 6	V-set and transmembrane domain-containing protein 2A	B5MCX6;F8W8J5;Q8TAG5;Q8TAG5-2;X6RBS5
H0YC04	V-type proton ATPase subunit B, brain isoform	H0YC04;P21281

Table 1 discloses proteins whose peptides were found to be regulated by at least 60% in the activated microglia cell line compared to resting cells and also at least 60% in the CSF of AD patients compared to CSF of non-AD subjects. Uniprot ID = annotated ID during data search; Protein names = protein name/s given to matched sequence; All Uniprot matches = All Uniprot
5 IDs that match to the peptide sequence detected at the time of invention. Asterisk (*) indicates those proteins which were annotated as deleted as the entry has been removed from Uniprot (due to redundancy).

In one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
10 thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, or at least two or more, optionally at least three or all biomarkers selected from the group of Peroxiredoxin-1, MARCKS-related protein, Moesin and Actin or fragments thereof.

In another embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or

having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, or at least two or more, optionally at least three or all biomarkers selected from the group of Peroxiredoxin-1, MARCKS-related protein, Moesin, Actin, Protein TMSB4XP4, ApoE, Gelsolin, Secretogranin, Albumin and complement proteins or fragments thereof.

In one embodiment the biomarker panel comprises phosphoglucosyltransferase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, optionally two or more biomarkers selected from Table 1 and/or Table 2 or fragments thereof.

TABLE 2

<u>Uniprot ID</u>	<u>Protein Name</u>	<u>All Uniprot matches</u>
G3V1C1	1,5-anhydro-D-fructose reductase (Aldo-keto reductase family 1, member C-like 2, isoform CRA_c)	G3V1C1;Q96JD6;Q96JD6-4;P14550
B8ZZ54	10 kDa heat shock protein, mitochondrial (Heat shock 10kDa protein 1 (Chaperonin 10), isoform CRA_h)	B8ZZ54;B8ZZL8;P61604
P31946	14-3-3 protein beta/alpha (Protein 1054) (Protein kinase C inhibitor protein 1) (KCIP-1) [Cleaved into: 14-3-3 protein beta/alpha, N-terminally processed]	P31946;P31946-2;P61981;Q4VY19;Q4VY20
A2IDB1	14-3-3 protein eta	A2IDB1;B4DJF2;E5RIR4;E7ESK7;E7EVZ2;E7EX29;E9PD24;E9PG15;F8WEB6;I3L0W5;I3L3T1;P27348;P31946;P31946-2;P31947;P31947-2;P61981;P62258;P63104;Q04917;Q4VY19;Q4VY20;E5RGE1
P61981	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1) [Cleaved into: 14-3-3 protein gamma, N-terminally processed]	P61981
E9PG15	14-3-3 protein theta	E9PG15;P27348
B0AZS6	14-3-3 protein zeta/delta (cDNA, FLJ79516, highly similar to 14-3-3 protein zeta/delta)	B0AZS6;B7Z2E6;E7EX29;H0YB80;P63104;P63104-2
P16885	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-2 (EC 3.1.4.11) (Phosphoinositide phospholipase C-gamma-2) (Phospholipase C-IV) (PLC-IV) (Phospholipase C-gamma-2) (PLC-gamma-2)	P16885
P62333	26S protease regulatory subunit 10B (26S proteasome AAA-ATPase subunit RPT4) (Proteasome 26S subunit ATPase 6) (Proteasome subunit p42)	H0YJC0;H0YJS8;P62332
P62191	26S protease regulatory subunit 4 (P26s4) (26S proteasome AAA-ATPase subunit RPT2) (Proteasome 26S subunit ATPase 1)	P62191-2;P62191

E9PKD5	26S protease regulatory subunit 6A	E9PKD5;E9PM69;P17980;R4GNH3;E9PM D8;E9PN50
P43686	26S protease regulatory subunit 6B (26S proteasome AAA-ATPase subunit RPT3) (MB67-interacting protein) (MIP224) (Proteasome 26S subunit ATPase 4) (Tat-binding protein 7) (TBP-7)	P43686
B7Z5E2	26S protease regulatory subunit 7#	B7Z5E2;P35998
J3KRP2	26S protease regulatory subunit 8	J3KRP2;J3QLH6;J3QQM1;J3QRR3;J3QS A9;P62195;P62195-2
C9J9M4	26S proteasome non-ATPase regulatory subunit 1	C9J9M4;H7BZR6;Q99460;Q99460-2
E9PL38	26S proteasome non-ATPase regulatory subunit 13	E9PL38;Q9UNM6;Q9UNM6-2
O00487	26S proteasome non-ATPase regulatory subunit 14 (EC 3.4.19.-) (26S proteasome regulatory subunit RPN11) (26S proteasome-associated PAD1 homolog 1)	O00487
H7C1H2	26S proteasome non-ATPase regulatory subunit 2	Q13200-3;Q13200-2;H7C1H2;Q13200
B4DT72	26S proteasome non-ATPase regulatory subunit 3 (cD FLJ54148, highly similar to 26S proteasome non-ATPase regulatory subunit 3)	B4DT72;H0YGV8;O43242
Q16401	26S proteasome non-ATPase regulatory subunit 5 (26S protease subunit S5 basic) (26S proteasome subunit S5B)	Q16401;Q16401-2;Q4VXG9
Q13442	28 kDa heat- and acid-stable phosphoprotein (PDGF-associated protein) (PAP) (PDGFA-associated protein 1) (PAP1)	Q13442
O75600	2-amino-3-ketobutyrate coenzyme A ligase, mitochondrial (AKB ligase) (EC 2.3.1.29) (Aminoacetone synthase) (Glycine acetyltransferase)	O75600;O75600-2
A6NF51	3'(2'),5'-bisphosphate nucleotidase 1	A6NF51;O95861-3;O95861-4;O95861;O95 861-2
E5RHF4	39S ribosomal protein L15, mitochondrial	E5RHF4;Q9P015
E7ESL0	39S ribosomal protein L22, mitochondrial	E7ESL0;J3KQY1;Q9NWU5;Q9NWU5-2;Q 9NWU5-3
B5MD38	3-ketoacyl-CoA thiolase	P55084-2;B5MD38;F5GZQ3;P55084;C9JE 81;C9JEY0
C9JDE9	3-ketoacyl-CoA thiolase, peroxisomal	C9JDE9;H7C131;P09110
F6U211	40S ribosomal protein S10	F6U211;P46783;S4R435
M0QZC5	40S ribosomal protein S11	M0QZC5;M0R1H6;P62280
P25398	40S ribosomal protein S12	P25398
P62277	40S ribosomal protein S13	P62277
K7EJ78	40S ribosomal protein S15	K7EJ78;K7ELC2;K7EM56;K7EQJ5;P6284 1;S4R456
I3L3P7	40S ribosomal protein S15a	I3L3P7;P62244
P62269	40S ribosomal protein S18 (Ke-3) (Ke3)	P62269
P39019	40S ribosomal protein S19	M0QXK4;M0QYF7;M0R140;M0R2L9;P390 18
E9PQD7	40S ribosomal protein S2	E9PQD7;H0YEN5;P15880
G3XAN0	40S ribosomal protein S20 (Ribosomal protein S20, isoform CRA_a)	G3XAN0;P60866;P60866-2
D6R9I7	40S ribosomal protein S23	D6R9I7;D6RD47;D6RDJ2;D6RIX0;P62266

E7ETK0	40S ribosomal protein S24	E7ETK0;P62847;P62847-2;P62847-3;P62847-4
P62851	40S ribosomal protein S25	P62851
P62854	40S ribosomal protein S26	P62854;Q5JNZ5
C9J1C5	40S ribosomal protein S27	C9J1C5;H0YMV8;P42677;Q71UM5
P62273	40S ribosomal protein S29	P62273;P62273-2
E9PL09	40S ribosomal protein S3	E9PL09;E9PPU1;E9PSF4;H0YEU2;P23396;P23396-2
A6NH36	40S ribosomal protein S4, X isoform	A6NH36;C9JEH7;P22090;P62701;Q8TD47
M0QZN2	40S ribosomal protein S5	M0QZN2;M0R0F0;M0R0R2;P46782
A2A3R5	40S ribosomal protein S6	A2A3R5;P62753
P46781	40S ribosomal protein S9 (Ribosomal protein S9, isoform CRA_c)	B5MCT8;C9JM19;P46780
A6NE09	40S ribosomal protein SA (37 kDa laminin receptor precursor) (37/67 kDa laminin receptor) (67 kDa laminin receptor) (Laminin receptor 1) (Laminin-binding protein precursor p40)	A6NE09;P08865;C9J9K3
F5GZI0	4F2 cell-surface antigen heavy chain	F5GZI0;F5GZS6;J3KPF3;P08195;P08195-2;P08195-3;P08195-4
P49189	4-trimethylaminobutyraldehyde dehydrogenase (TMABADH) (EC 1.2.1.47) (Aldehyde dehydrogenase E3 isozyme) (Aldehyde dehydrogenase family 9 member A1) (EC 1.2.1.3) (Gamma-aminobutyraldehyde dehydrogenase) (EC 1.2.1.19) (R-aminobutyraldehyde dehydrogenase)	P49189
B7Z712	60 kDa heat shock protein, mitochondrial#	B7Z712;C9JCQ4;C9JL19;C9JL25;E7ESH4;E7EXB4;P10809
F8VQY6	60S acidic ribosomal protein P0	F8VQY6;F8VRK7;F8VS58;F8VU65;F8VWS0;F8VZS0;G3V210;P05388;P05388-2;Q8NHW5
F8W7C6	60S ribosomal protein L10	A6QR19;F8W7C6;H7C123;H7C2C5;P27635;Q96L21;X1WI27
P62906	60S ribosomal protein L10a (CSA-19) (Neural precursor cell expressed developmentally down-regulated protein 6) (NEDD-6)	P62906
P62913	60S ribosomal protein L11 (CLL-associated antigen KW-12)	P62913;P62913-2;Q5VVC8;Q5VVC9
P26373	60S ribosomal protein L13 (Breast basic conserved protein 1)	J3KS98;P26373;P26373-1
M0QYS1	60S ribosomal protein L13a	M0QYS1;P40429
J3KRB3	60S ribosomal protein L17	J3KRX5;J3QLC8;J3QQT2;J3QS96;P18621;P18621-2;P18621-3;J3KRB3
F8VYV2	60S ribosomal protein L18	Q07020-2;F8VYV2;G3V203;H0YHA7;J3QQ67;Q07020
M0R0P7	60S ribosomal protein L18a	M0R0P7;M0R117;M0R1A7;M0R3D6;Q02543
G3V1B3	60S ribosomal protein L21 (Ribosomal protein L21, isoform CRA_f)	G3V1B3;M0R181;P46778
K7EJT5	60S ribosomal protein L22	K7EJT5;K7EKS7;K7ELC4;K7EMH1;K7EP65;K7ERI7;P35268
C9JYQ9	60S ribosomal protein L22-like 1	C9JYQ9;H0Y8C2;Q6P5R6
B9ZVP7	60S ribosomal protein L23	B9ZVP7;C9JD32;J3KT29;P62829
A8MUS3	60S ribosomal protein L23a (Ribosomal protein L23a, isoform CRA_a)	A8MUS3;H7BY10;K7EJV9;K7EMA7;K7ERT8;P62750

E5RIT6	60S ribosomal protein L26-like 1	E5RIT6;J3QQQ9;J3QQV1;J3QRC4;J3QRI7;P61254;Q9UNX3;J3KTJ8
F8WCR1	60S ribosomal protein L3	F8WCR1;H7C3M2;H7C422;P39023;B5MCW2;G5E9G0
G5E9G0	60S ribosomal protein L3 (Ribosomal protein L3, isoform CRA_e) (Uncharacterized protein)	G5E9G0;P39023;Q92901
B7Z4C8	60S ribosomal protein L31 (cDNA FLJ57527, highly similar to 60S ribosomal protein L31)	B7Z4C8;B7Z4E3;B8ZZK4;C9JU56;H7C2W9;P62899;P62899-2;P62899-3
D3YTB1	60S ribosomal protein L32	D3YTB1;F8W727;P62910
P49207	60S ribosomal protein L34	P49207
Q9Y3U8	60S ribosomal protein L36	Q9Y3U8
P61927	60S ribosomal protein L37 (G1.16)	P61927
P63173	60S ribosomal protein L38	P63173
H3BM89	60S ribosomal protein L4 (Ribosomal protein L4, isoform CRA_a)	H3BM89;P36578
P46777	60S ribosomal protein L5	P46777
Q02878	60S ribosomal protein L6 (Neoplasm-related protein C140) (Tax-responsive enhancer element-binding protein 107) (TaxREB107)	Q02878
P62424	60S ribosomal protein L7a (PLA-X polypeptide) (Surfeit locus protein 3)	P62424;Q5T8U2;Q5T8U3
E9PKU4	60S ribosomal protein L8	E9PKZ0;G3V1A1;P62917;E9PKU4
D6RAN4	60S ribosomal protein L9	H0Y9R4;H0Y9V9;P32969;D6RAN4
M0R261	6-phosphogluconolactonase	M0R261;O95336
P11021	78 kDa glucose-regulated protein (GRP-78) (Endoplasmic reticulum lumel Ca(2+)-binding protein grp78) (Heat shock 70 kDa protein 5) (Immunoglobulin heavy chain-binding protein) (BiP)	P11021
H0YEL7	Acetyl-CoA acetyltransferase, mitochondrial	H0YEL7;P24752
Q5T0Y8	Acid sphingomyelinase-like phosphodiesterase 3b	Q5T0Y8;Q92485;Q92485-2
P60709	Actin, cytoplasmic 1 (Beta-actin) [Cleaved into: Actin, cytoplasmic 1, N-terminally processed]	G5E9R0;I3L1U9;I3L3R2;J3KT65;K7EM38;P60709;P63261;E7EVS6;I3L4N7
I3L4N8	Actin, cytoplasmic 2	P60709;P63261;Q6S8J3;I3L4N8
I3L1U9	Actin, cytoplasmic 2, N-terminally processed	I3L1U9;P60709;P63261;I3L4N8
O94805	Actin-like protein 6B (53 kDa BRG1-associated factor B) (Actin-related protein Baf53b) (ArpNalpha) (BRG1-associated factor 53B) (BAF53B)	O94805;O96019;O96019-2
F5H6T1	Actin-related protein 2	F5H6T1;P61160;P61160-2
P61160	Actin-related protein 2 (Actin-like protein 2)	P61160;P61160-2
O15143	Actin-related protein 2/3 complex subunit 1B (Arp2/3 complex 41 kDa subunit) (p41-ARC)	C9J4Z7;C9J6C8;C9JBJ7;C9JEY1;C9JTT6;C9K057;O15142
B1ALC0	Actin-related protein 2/3 complex subunit 5	B1ALC0;O15511;O15511-2;Q9BPX5
B4DXW1	Actin-related protein 3 (cDNA FLJ51148, highly similar to Actin-like protein 3) (cDNA FLJ52434, highly similar to Actin-like protein 3) (cDNA, FLJ79112, highly similar to Actin-like protein 3) (cDNA, FLJ79295, highly similar to Actin-like protein 3)	B4DXW1;F5H3P5;P61158
G3V3W9	Activator of 90 kDa heat shock protein ATPase	O95433-2;G3V3W9;O95433

	homolog 1	
B7Z683	Active breakpoint cluster region-related protein (cDNA FLJ54747, highly similar to Active breakpoint cluster region-related protein)	B7Z683;Q12979;Q12979-2;Q12979-4;I3L434;I3NI05;Q12979-3
G3V2U7	Acylphosphatase (EC 3.6.1.7)	G3V2U7;P07311
O95372	Acyl-protein thioesterase 2 (APT-2) (EC 3.1.2.-) (Lysophospholipase II) (LPL-II) (LysoPLA II)	O95372;Q5QPQ0
B5MDS5	Adenomatous polyposis coli protein 2	B5MDS5;O95996;O95996-2;O95996-3
P23526	Adenosylhomocysteinase (AdoHcyase) (EC 3.3.1.1) (S-adenosyl-L-homocysteine hydrolase)	P23526;P23526-2
E7ERF4	Adenylosuccite lyase	E7ERF4;P30566;P30566-2
G3V232	Adenylosuccite synthetase isozyme 1	G3V232;G3V5D8;Q8N142;Q8N142-2
Q01518	Adenylyl cyclase-associated protein 1 (CAP 1)	Q01518;Q01518-2
H0Y512	Adipocyte plasma membrane-associated protein	H0Y512;Q9HDC9;Q9HDC9-2
P05141	ADP/ATP translocase 2 (ADP,ATP carrier protein 2) (ADP,ATP carrier protein, fibroblast isoform) (Adenine nucleotide translocator 2) (ANT 2) (Solute carrier family 25 member 5) [Cleaved into: ADP/ATP translocase 2, N-terminally processed]	P05141
I7HJJ0	ADP/ATP translocase 3	I7HJJ0;P05141;P12235;P12236;Q9H0C2;V9GYG0
B7ZB63	ADP-ribosylation factor 3 (cDNA, FLJ79427, highly similar to ADP-ribosylation factor 3)	B7ZB63;C9J1Z8;C9JPM4;F5H0C7;F5H1V1;F5H423;F5H6T5;F8WDB3;P18085;P61204;P84077;P84085
B0QYR5	ADP-ribosylation factor-binding protein GGA1	B0QYR5;B0QYR6;B0QYR9;B0QYS0;B0QYS1;B0QYS3;B0QYS5;B7Z1E9;H3BMM6;H3BPI3;J3KSS7;J3QRP3;J3QRS8;Q6IC75;Q9NZ52;Q9NZ52-4;Q9UJY4;Q9UJY5;Q9UJY5-3;Q9UJY5-4;B0QYS2
Q96BM9	ADP-ribosylation factor-like protein 8A (ADP-ribosylation factor-like protein 10B) (Novel small G protein indispensable for equal chromosome segregation 2)	Q96BM9;Q9NVJ2
B4DI85	ADP-ribosylation factor-like protein 8B#	B4DI85;Q9NVJ2;Q96BM9
F8VUB6	Aladin	F8VUB6;F8VZ44;H3BU82;Q9NRG9;Q9NRG9-2
H3BPK7	Alanine--tRNA ligase, cytoplasmic	H3BPK7;P49588
P14550	Alcohol dehydrogenase [NADP(+)] (EC 1.1.1.2) (Aldehyde reductase) (Aldo-keto reductase family 1 member A1)	P14550;Q5T621;V9GYG2;V9GYP9
H0YAG8	Alcohol dehydrogenase class-3	H0YAG8;P11766
H0Y2X5	Aldehyde dehydrogenase 1 family, member A3, isoform CRA_b (Aldehyde dehydrogenase family 1 member A3)	H0Y2X5;H0YMG7;O94788;O94788-2;O94788-3;O94788-4;P00352;P05091;P05091-2;P30837;P47895
P05091	Aldehyde dehydrogenase, mitochondrial (EC 1.2.1.3) (ALDH class 2) (ALDH-E2) (ALDHI)	P05091;P05091-2;S4R3S4
B8ZZ75	Aldose 1-epimerase	B8ZZ75;H7C1B5;Q96C23
E9PCX2	Aldose reductase	E9PCX2;E9PEF9;P15121
P15121	Aldose reductase (AR) (EC 1.1.1.21) (Aldehyde reductase) (Aldo-keto reductase family 1 member B1)	P15121
P02763	Alpha-1-acid glycoprotein 1 (AGP 1) (Orosomucoid-1) (OMD 1)	P02763

P19652	Alpha-1-acid glycoprotein 2 (AGP 2) (Orosomucoid-2) (OMD 2)	P19652
P30533	Alpha-2-macroglobulin receptor-associated protein (Alpha-2-MRAP) (Low density lipoprotein receptor-related protein-associated protein 1) (RAP)	P30533
G3V2E8	Alpha-actinin-1	P35609-2;G3V2E8;G3V2W4;G3V2X9;G3V5M4;H9KV75;P12814;P12814-2;P12814-3;P12814-4;P35609;G3V2N5
C9J196	Alpha-dystroglycan	Q14118;C9J196;C9JQL4
M0R0I4	Alpha-soluble NSF attachment protein	M0R0I4;M0R2M1;P54920
A6NKB8	Aminopeptidase B	A6NKB8;C9JMZ3;Q9H4A4
B7Z4G8	Amyloid-like protein 1 (cDNA FLJ56046, highly similar to Amyloid-like protein 1 (APLP)(APLP-1))	B7Z4G8;F5GZ08;K7ELK0;K7EQJ4;P51693;P51693-2
P04083	Annexin A1 (Annexin I) (Annexin-1) (Calpactin II) (Calpactin-2) (Chromobindin-9) (Lipocortin I) (Phospholipase A2 inhibitory protein) (p35)	P04083
B4DDF9	Annexin A4#	B4DDF9;P09525;Q6P452
P01008	Antithrombin-III (ATIII) (Serpine C1)	P01008
C9J1E7	AP-1 complex subunit beta-1	C9J1E7;Q10567;Q10567-2;Q10567-3;Q10567-4
O94973	AP-2 complex subunit alpha-2 (100 kDa coated vesicle protein C) (Adaptor protein complex AP-2 subunit alpha-2) (Adaptor-related protein complex 2 subunit alpha-2) (Alpha-adaptin C) (Alpha2-adaptin) (Clathrin assembly protein complex 2 alpha-C large chain) (Huntingtin yeast partner J) (Huntingtin-interacting protein 9) (HIP-9) (Huntingtin-interacting protein J) (Plasma membrane adaptor HA2/AP2 adaptin alpha C subunit)	O94973;O94973-2;O94973-3;O95782;O95782-2
K7EJT8	AP-2 complex subunit beta	K7EJT8;P63010;P63010-2;P63010-3
P02649	Apolipoprotein E (Apo-E)	E7ERP7;E9PEV4;H0Y7L5;P02648
E9PMA0	Apoptosis-inducing factor 1, mitochondrial	E9PMA0;O95831;O95831-2;O95831-3;O95831-5
C9JLV4	Apoptotic protease-activating factor 1	C9JLV4;O14727;O14727-2;O14727-3;O14727-4;O14727-5;Q53F19;Q53F19-2
P20292	Arachidate 5-lipoxygenase-activating protein (FLAP) (MK-886-binding protein)	P20292
B0YIW6	Archain 1, isoform CRA_a (Coatomer subunit delta) (Coatomer subunit delta variant 2)	B0YIW6;P48444;P48444-2
O43150	Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 2 (Development and differentiation-enhancing factor 2) (Paxillin-associated protein with ARF GAP activity 3) (PAG3) (Pyk2 C-terminus-associated protein) (PAP)	O43150;O43150-2
F5H3T8	Arginine--tR ligase, cytoplasmic	F5H3T8;P54136;P54136-2
P05089	Arginase-1 (EC 3.5.3.1) (Liver-type arginase) (Type I arginase)	P05089;P05089-2;P05089-3
P08243	Asparagine synthetase [glutamine-hydrolyzing] (EC 6.3.5.4) (Cell cycle control protein TS11) (Glutamine-dependent asparagine synthetase)	P08243;P08243-2;P08243-3
O43776	Asparagine--tRNA ligase, cytoplasmic (EC	O43776

	6.1.1.22) (Asparaginyl-tRNA synthetase) (AsnRS)	
H7BZ35	Aspartate--tRNA ligase, cytoplasmic	P14868;Q68CR9;H7BZ35
B1AKZ3	Astrocytic phosphoprotein PEA-15 (Phosphoprotein enriched in astrocytes 15, isoform CRA_b) (cD FLJ38560 fis, clone HCHON2003642, highly similar to Astrocytic phosphoprotein PEA-15)	B1AKZ3;B1AKZ5;Q15121
D6R9H7	ATP synthase F(0) complex subunit C1, mitochondrial	D6R9H7;E7EPU7;E7EQ97;I3L0Y5;P05496;P48201;Q06055;Q06055-2;Q06055-3
P25705	ATP synthase subunit alpha, mitochondrial	K7EK77;K7ENJ4;P25705-3;K7ERX7;P25705;P25705-2;K7EJP0
B4DL14	ATP synthase subunit gamma	B4DL14;P36542;P36542-2
H0Y2W2	ATPase family AAA domain-containing protein 3A	H0Y2W2;J3QSF3;Q5T2N8;Q5T9A4;Q5T9A4-2;Q5T9A4-3;Q9NVI7;Q9NVI7-2;Q9NVI7-3
G3V126	ATPase, H ⁺ transporting, lysosomal 50/57kDa, V1 subunit H, isoform CRA_c (V-type proton ATPase subunit H)	G3V126;Q9UI12;Q9UI12-2
B4E3P0	ATP-citrate synthase (cDNA FLJ55447, highly similar to ATP-citrate synthase (EC 2.3.3.8))	B4E3P0;P53396;P53396-2
B1APP6	ATP-dependent 6-phosphofructokinase, platelet type	B1APP6;Q01813;Q01813-2
Q08211	ATP-dependent RNA helicase A (RHA) (EC 3.6.4.13) (DEAH box protein 9) (Leukophysin) (LKP) (Nuclear DNA helicase II) (NDH II)	Q08211
B1Q2N1	ATP-dependent RNA helicase DDX39A (DEAD (Asp-Glu-Ala-Asp) box polypeptide 39 transcript variant)	B1Q2N1;B4DIJ6;B4DP52;F6S4E6;F6TRA5;F6UJC5;F6WLT2;F8VQ10;K7EPJ3;K7EQN7;O00148;O00148-2;Q13838;Q13838-2;Q5STU3
B4DLA0	ATP-dependent RNA helicase DDX3X (cDNA FLJ55031, highly similar to ATP-dependent RNA helicase DDX3X (EC 3.6.1.-))	B4DLA0;B4E3C4;O00571
B5MCE7	Basic leucine zipper and W2 domain-containing protein 2 (Basic leucine zipper and W2 domains 2, isoform CRA_b)	B5MCE7;B5MCH7;E7ETZ4;Q75MG1;Q9Y6E2
P51572	B-cell receptor-associated protein 31 (BCR-associated protein 31) (Bap31) (6C6-AG tumor-associated antigen) (Protein CDM) (p28)	P51572;P51572-2
J3KRP0	Beta-Ala-His dipeptidase	J3KRP0;Q96KN2
P32121	Beta-arrestin-2 (Arrestin beta-2)	P32121;P32121-2;P32121-3;P32121-4;P32121-5;Q68DZ5
A2A2P1	Beta-catenin-like protein 1	A2A2P1;Q8WYA6-4;Q8WYA6
P42025	Beta-centractin (Actin-related protein 1B) (ARP1B)	P42025;P61163;R4GMT0
P13929	Beta-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hydro-lyase) (Enolase 3) (Muscle-specific enolase) (MSE) (Skeletal muscle enolase)	P13929;P13929-2;P13929-3
B4DKE7	Beta-hexosaminidase subunit alpha#	B4DKE7;E9PGL4;H3BP20;H3BS10;H3BT D4;H3BU85;P06865
P07686	Beta-hexosaminidase subunit beta (EC 3.2.1.52) (Beta-N-acetylhexosaminidase subunit beta) (Hexosaminidase subunit B) (Cervical cancer proto-oncogene 7 protein) (HCC-7) (N-acetyl-beta-glucosaminidase subunit beta)	P07686;Q5URX0

	[Cleaved into: Beta-hexosaminidase subunit beta chain B; Beta-hexosaminidase subunit beta chain A]	
P07814	Bifunctional glutamate/proline--tRNA ligase (Bifunctional aminoacyl-tRNA synthetase) (Cell proliferation-inducing gene 32 protein) (Glutamyl-prolyl-tRNA synthetase) [Includes: Glutamate--tRNA ligase (EC 6.1.1.17) (Glutamyl-tRNA synthetase) (GluRS); Proline--tRNA ligase (EC 6.1.1.15) (Prolyl-tRNA synthetase)]	P07814;V9GYZ6
H7C3X0	Bifunctional protein NCOAT	O60502-4;H7C3X0;O60502;O60502-2;O60502-3
Q96GW7	Brevican core protein (Brain-enriched hyaluronan-binding protein) (BEHAB) (Chondroitin sulfate proteoglycan 7)	Q5T3I7;Q96GW7;Q96GW7-1
F5H2F4	C-1-tetrahydrofolate synthase, cytoplasmic	F5H2F4;P11586
Q9Y376	Calcium-binding protein 39 (MO25alpha) (Protein Mo25)	Q9Y376
B7ZBJ4	Calcium-binding protein 39-like	B7ZBJ4;Q5TAW7;Q9H9S4;Q9Y376
E7ERY9	Calcium-transporting ATPase (EC 3.6.3.8)	E7ERY9;P20020;P20020-2;P20020-3;P20020-4;P20020-5;P20020-6
Q9HB71	Calcyclin-binding protein (CacyBP) (hCacyBP) (S100A6-binding protein) (Siah-interacting protein)	Q9HB71;Q9HB71-3
D6RAQ8	Calnexin	P27824-2;D6RAQ8;D6RAU8;D6RB85;D6RDP7;H0Y9Q7;P27824
P27797	Calreticulin (CRP55) (Calregulin) (Endoplasmic reticulum resident protein 60) (ERp60) (HACBP) (grp60)	K7EJB9;K7EL50;P27796
O94985	Calsyntenin-1 (Alcadein-alpha) (Alc-alpha) (Alzheimer-related cadherin-like protein) (Non-classical cadherin XB31alpha) [Cleaved into: Soluble Alc-alpha (SAlc-alpha); CTF1-alpha (C-terminal fragment 1-alpha)]	O94985-2
O43852	Calumenin (Crocabin) (IEF SSP 9302)	O43852;O43852-10;O43852-15;O43852-2;O43852-3;O43852-4;O43852-6;O43852-8
P10644	cAMP-dependent protein kinase type I-alpha regulatory subunit (Tissue-specific extinguisher 1) (TSE1) [Cleaved into: cAMP-dependent protein kinase type I-alpha regulatory subunit, N-terminally processed]	P10644
H7BYW5	cAMP-dependent protein kinase type I-beta regulatory subunit	H7BYW5;P10644;P31321
H7C4A9	cAMP-dependent protein kinase type II-alpha regulatory subunit	H7C4A9;P13861;Q9BUB1
K7EID3	cAMP-dependent protein kinase type I-alpha regulatory subunit	K7EID3;K7EIE5;K7EJ40;K7EK41;K7ENR3;K7EPB2;K7ER48;P10644
B1AK87	Capping protein (Actin filament) muscle Z-line, beta, isoform CRA_a (F-actin-capping protein subunit beta)	B1AK87;B1AK88;P47756;P47756-2
A8MTM1	Carbonyl reductase [NADPH] 1	A8MTM1;P16152-2;E9PQ63;P16152
C9JE88	Carboxypeptidase E	C9JE88;D6R930;D6RF88;P16870;P16870-2
H3BSA1	Casein kinase II subunit alpha	H3BSA1;H3BV19;P19784
C9JZR2	Catenin delta-1	C9JZR2;E9PKY0;O60716;O60716-10;O60

		716-11;O60716-12;O60716-13;O60716-14;O60716-15;O60716-16;O60716-17;O60716-18;O60716-19;O60716-2;O60716-20;O60716-21;O60716-22;O60716-23;O60716-24;O60716-25;O60716-26;O60716-27;O60716-28;O60716-29;O60716-3;O60716-30;O60716-31;O60716-32;O60716-4;O60716-5;O60716-6;O60716-7;O60716-8;O60716-9
P43235	Cathepsin K (EC 3.4.22.38) (Cathepsin O) (Cathepsin O2) (Cathepsin X)	P43235;Q5QP40
Q9UBR2	Cathepsin Z (EC 3.4.18.1) (Cathepsin P) (Cathepsin X)	Q9UBR2
F5GXJ9	CD166 antigen	F5GXJ9;H7C543;Q13740;Q13740-2;Q13740-4
Q9NZ45	CDGSH iron-sulfur domain-containing protein 1 (MitoNEET)	Q9NZ45
B3KRG5	cDNA FLJ34201 fis, clone FCBBF3019714, highly similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN G	B3KRG5;H3BUY5;P38159;P38159-2;Q96E39
B7Z514	cDNA FLJ50601, highly similar to Glutathione synthetase (EC 6.3.2.3)	B7Z514;P48637
B7Z3E2	cDNA FLJ50777, highly similar to Serine/threonine-protein phosphatase 6 (EC 3.1.3.16) (cDNA, FLJ79426, highly similar to Serine/threonine-protein phosphatase 6 (EC 3.1.3.16))	B7Z3E2;O00743;O00743-2;O00743-3
B4DXI8	cDNA FLJ51373, highly similar to 26S proteasome non-ATPase regulatory subunit 7	B4DXI8;H3BNT7;H3BTM8;P51665
B4DPJ8	cDNA FLJ52344, highly similar to T-complex protein 1 subunit zeta (cDNA, FLJ79129, highly similar to T-complex protein 1 subunit zeta)	B4DPJ8;P40227;P40227-2
B4DN60	cDNA FLJ52703, highly similar to Asparaginyl-tRNA synthetase, cytoplasmic (EC6.1.1.22)	B4DN60;O43776
B4DTM7	cDNA FLJ53006, highly similar to Vinculin	B4DTM7;P18206;P18206-2;P18206-3
B4DUC5	cDNA FLJ53202, highly similar to Exportin-2	B4DUC5;P55060;P55060-3;P55060-4
B4DT31	cDNA FLJ53425, highly similar to Far upstream element-binding protein 1	B4DT31;E9PEB5;M0R0I5;Q92945;Q96AE4;Q96AE4-2;Q96I24;Q96I24-2
B7Z2F4	cDNA FLJ53873, highly similar to T-complex protein 1 subunit delta	B7Z2F4;B7Z9L0;P50991;P50991-2
B4DX42	cDNA FLJ54064, highly similar to Splicing factor 1	B4DX42;Q15637;Q15637-2;Q15637-3;Q15637-4;Q15637-6;Q15637-7;Q15637-5
B4DTC3	cDNA FLJ54150, highly similar to Heterogeneous nuclear ribonucleoprotein D0	B4DTC3;F5H6R6;H0YA96;Q14103;Q14103-2;Q14103-3;Q14103-4;H0Y8G5
B4E2J1	cDNA FLJ54240, highly similar to ATPase family AAA domain-containing protein 1	B4E2J1;Q8NBU5
B4DYV7	cDNA FLJ54806, highly similar to Homo sapiens meningioma expressed antigen 5 (MGEA5), mRNA	B4DYV7;O60502-4;H7C3X0;O60502;O60502-2;O60502-3
B4DG22	cDNA FLJ56618, highly similar to Ribosomal protein S6 kinase alpha-3 (EC 2.7.11.1)	B4DG22;B7Z3B5;B7ZB17;B7ZL90;E9PGT3;E9PRI4;F2Z2J1;F5GYC4;P51812;Q15349;Q15349-2;Q15349-3;Q15418;Q15418-2;Q15418-3;Q5SVM6;Q9UK32
B1APJ0	cDNA FLJ57459, highly similar to Mitochondrial import inner membrane translocase subunit Tim23	B1APJ0;E7EP42;E9PB91;O14925;Q5SRD1;S4R2X5
B7Z8M7	cDNA FLJ57768, highly similar to Ras-related	B7Z8M7;E7END7;P62820;P62820-2

	protein Rab-1A	
B4DDM6	cDNA FLJ57899, highly similar to Mitotic checkpoint protein BUB3	B4DDM6;J3QT28;O43684;O43684-2
B4DIZ2	cDNA FLJ57995, moderately similar to Ubiquitin-conjugating enzyme E2-25 kDa (EC 6.3.2.19)	B4DIZ2;D6RDM7;P61086;P61086-3
B7Z1Z6	cDNA FLJ58056, highly similar to Calcium/calmodulin-dependent protein kinase type II beta chain (EC 2.7.11.17)	D6R938;E9PBG7;E9PF82;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9;B7Z1Z6;D6RHX9;E7EQE4;E9PBE8;H7BXS4;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
B4DLC0	cDNA FLJ58476, highly similar to Poly(rC)-binding protein 2	B4DLC0;B4DXP5;F8VRH0;F8VXH9;F8VZX2;Q15366-7;H3BRU6;Q15366;Q15366-2;Q15366-3;Q15366-4;Q15366-5;Q15366-6
B7Z5N7	cDNA FLJ58612, highly similar to Sec1 family domain-containing protein 1	B7Z5N7;B7Z738;Q8WVM8;Q8WVM8-2;Q8WVM8-3
B4DJ96	cDNA FLJ59548, highly similar to Cisplatin resistance-associated overexpressed protein	B4DJ96;D6RDI2;J3KPP4;O95232
B4DKM5	cDNA FLJ60120, highly similar to Voltage-dependent anion-selective channel protein 2 (cDNA, FLJ78818, highly similar to Voltage-dependent anion-selective channel protein 2)	B4DKM5;P45880;P45880-1;P45880-2
B4DH61	cDNA FLJ60521, highly similar to Protein kinase-like protein C9orf96	E9PKD5;E9PM69;P17980;R4GNH3;B4DH61;E9PLG2;E9PMD8;E9PN50
A8K8G0	cDNA FLJ75113	A8K8G0;P51858;P51858-2;P51858-3
B7Z9J8	cDNA, FLJ78862, highly similar to Isocitrate dehydrogenase (cDNA, FLJ78950, highly similar to Isocitrate dehydrogenase)	B7Z9J8;H0YL72;H0YMU3;P50213;P50213-2
Q9BY67	Cell adhesion molecule 1 (Immunoglobulin superfamily member 4) (IgSF4) (Nectin-like protein 2) (NECL-2) (Spermatogenic immunoglobulin superfamily) (SgIgSF) (Synaptic cell adhesion molecule) (SynCAM) (Tumor suppressor in lung cancer 1) (TSLC-1)	Q9BY67;Q9BY67-2;Q9BY67-3;Q9BY67-4;Q9BY67-5;X5DQS5
Q8NFZ8	Cell adhesion molecule 4 (Immunoglobulin superfamily member 4C) (IgSF4C) (Nectin-like protein 4) (NECL-4) (TSLC1-like protein 2)	Q8NFZ8
E7ETU3	Cell division control protein 42 homolog	E7ETU3;P60953
E7ETU3	Cell division control protein 42 homolog*	E7ETU3;P60953;P60953-1;Q5JYX0
E9PFZ2	Ceruloplasmin	E9PFZ2;H7C5R1;P00450
Q7LBR1	Charged multivesicular body protein 1b (CHMP1.5) (Chromatin-modifying protein 1b) (CHMP1b) (Vacuolar protein sorting-associated protein 46-2) (Vps46-2) (hVps46-2)	Q7LBR1
Q9H444	Charged multivesicular body protein 4b (Chromatin-modifying protein 4b) (CHMP4b) (SNF7 homolog associated with Alix 1) (SNF7-2) (hSnf7-2) (Vacuolar protein sorting-associated protein 32-2) (Vps32-2) (hVps32-2)	Q9H444
O00299	Chloride intracellular channel protein 1 (Chloride	O00299

	channel ABP) (Nuclear chloride ion channel 27) (NCC27) (Regulatory nuclear chloride ion channel protein) (hRNCC)	
C9J050	Choline-phosphate cytidylyltransferase A	C9J050;C9JEJ2;H7BZN1;H7C1T3;P49585;C9J2E1
O95196	Chondroitin sulfate proteoglycan 5 (Acidic leucine-rich EGF-like domain-containing brain protein) (Neuroglycan C)	O95196;O95196-2
B8ZZ43	Chromobox homolog 3 (HP1 gamma homolog, Drosophila), isoform CRA_b (Chromobox protein homolog 3)	B8ZZ43;C9JMM0;Q13185;S4R2Y4
Q13185	Chromobox protein homolog 3 (HECH) (Heterochromatin protein 1 homolog gamma) (HP1 gamma) (Modifier 2 protein)	Q13185;S4R2Y4
F5GWX5	Chromodomain-helicase-DNA-binding protein 4	F5GWX5;Q12873;Q12873-2;Q12873-3;Q14839;Q14839-2
G5E968	Chromogranin-A (CgA) (Pituitary secretory protein I) (SP-I) [Cleaved into: Vasostatin-1 (Vasostatin I); Vasostatin-2 (Vasostatin II); EA-92; ES-43; Pancreastatin; SS-18; WA-8; WE-14; LF-19; AL-11; GV-19; GR-44; ER-37]	G5E968;P10645
B4DJV2	Citrate synthase	B4DJV2;F8VPA1;F8VTT8;F8VX07;F8VX68;F8W1S4;F8W4S1;F8W642;H0YH82;O75390;F8VFP9;F8VRP1;F8VZK9
Q00610	Clathrin heavy chain 1 (Clathrin heavy chain on chromosome 17) (CLH-17)	J3KRF5;J3KS13;K7EJJ5;Q00610;Q00610-1
Q14677	Clathrin interactor 1 (Clathrin-interacting protein localized in the trans-Golgi region) (Clint) (Enthoprotin) (Epsin-4) (Epsin-related protein) (EpsinR)	Q14677;Q14677-2;Q14677-3
F8WF69	Clathrin light chain A	F8WF69;P09496;P09496-2;P09496-3;P09496-4
P09497	Clathrin light chain B (Lcb)	P09497;P09497-2
I3L2B0	Clustered mitochondria protein homolog	I3L2B0;K7EIG1;O75153
E7ERK6	Clusterin beta chain	E7ERK6;H0YC35;H0YLK8;P10909;P10909-2;P10909-3;P10909-4;P10909-5
Q14019	Coactosin-like protein	Q14019
B4DZI8	Coatomer protein complex, subunit beta 2 (Beta prime), isoform CRA_b (Coatomer subunit beta') (cD FLJ56271, highly similar to Coatomer subunit beta)	B4DZI8;P35606
P53621	Coatomer subunit alpha (Alpha-coat protein) (Alpha-COP) (HEP-COP) (HEPCOP) [Cleaved into: Xenin (Xenopsin-related peptide); Proxenin]	P53621;P53621-2
B4DZI8	Coatomer subunit beta#	B4DZI8;P35606
F8VVA7	Coatomer subunit zeta-1	P61923-3;F8VVA7;P61923-4;F8VYK5;F8W651;P61923;P61923-2
E9PK25	Cofilin-1	E9PK25;G3V1A4;P23528;E9PP50
A6NNP5	Coiled-coil domain-containing protein 169	A6NNP5;A6NNP5-3;A6NNP5-4;A6NNP5-5;A6NNP5-6;E9PBZ7;H7C1A8;Q9GZT8;Q9GZT8-2;Q9NX45-3
C9JRZ6	Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial	C9JRZ6;F8WAR4;Q9NX63
E9PLT0	Cold shock domain-containing protein E1	E9PLT0;O75534-4;O75534;O75534-2;O75534-3
P12109	Collagen alpha-1(VI) chain	P12109

Q5KU26	Collectin-12 (Collectin placenta protein 1) (CL-P1) (hCL-P1) (Nurse cell scavenger receptor 2) (Scavenger receptor class A member 4) (Scavenger receptor with C-type lectin)	Q5KU26
P01024	Complement C3 (C3 and PZP-like alpha-2-macroglobulin domain-containing protein 1) [Cleaved into: Complement C3 beta chain; C3-beta-c (C3bc); Complement C3 alpha chain; C3a anaphylatoxin; Acylation stimulating protein (ASP) (C3adesArg); Complement C3b alpha' chain; Complement C3c alpha' chain fragment 1; Complement C3dg fragment; Complement C3g fragment; Complement C3d fragment; Complement C3f fragment; Complement C3c alpha' chain fragment 2]	M0QXZ3;P01023
F5GXS0	Complement C4-B	F5GXS0;P0C0L4;P0C0L4-2;P0C0L5
F8WDX4	Complement factor H	P08603;F8WDX4;P08603-2
Q12860	Contactin-1 (Glycoprotein gp135) (Neural cell surface protein F3)	Q12860;Q12860-2
C9JFE4	COP9 signalosome complex subunit 1 (G protein pathway suppressor 1, isoform CRA_b)	C9JFE4;J3KSA5;Q13098;Q13098-5;Q13098-6;Q13098-7
C9JLV5	COP9 signalosome complex subunit 3	H7C3P9;J3KTQ1;J3QKR0;Q9UNS2;Q9UNS2-2;C9JLV5
D6RAX7	COP9 signalosome complex subunit 4	D6RAX7;D6RFN0;Q9BT78;Q9BT78-2
E5RHH5	COP9 signalosome complex subunit 5 (SGN5) (Signalosome subunit 5) (EC 3.4.-.-) (Jun activation domain-binding protein 1)	E5RHH5;Q92905
O75131	Copine-3 (Copine III)	O75131
O75367	Core histone macro-H2A.1 (Histone macroH2A1) (mH2A1) (Histone H2A.y) (H2A/y) (Medulloblastoma antigen MU-MB-50.205)	O75367;O75367-2;O75367-3
H3BRY3	Coronin	H3BRY3;H3BTU6;P31146;H3BRJ1
Q9BR76	Coronin-1B (Coronin-2)	Q9BR76
D6RAX2	C-terminal-binding protein 1	E7EPF8;E7ESU7;P56545;P56545-2;Q13363;Q13363-2;Q5SQP8;D6RAX2
P17812	CTP synthase 1 (EC 6.3.4.2) (CTP synthetase 1) (UTP--ammonia ligase 1)	P17812-2;P17812
Q13616	Cullin-1 (CUL-1)	Q13616
Q13618	Cullin-3 (CUL-3)	Q13618;Q13618-2;Q13618-3
A6NE76	Cullin-4B	A6NE76;K4DI93;Q13620;Q13620-1;Q13620-3
Q86VP6	Cullin-associated NEDD8-dissociated protein 1 (Cullin-associated and neddylation-dissociated protein 1) (TBP-interacting protein of 120 kDa A) (TBP-interacting protein 120A) (p120 CAND1)	Q86VP6;Q86VP6-2
P01034	Cystatin-C (Cystatin-3) (Gamma-trace) (Neuroendocrine basic polypeptide) (Post-gamma-globulin)	P01034
F5GWD2	Cytochrome b-245 heavy chain	F5GWD2;F5GWU5;P04839;Q9Y5S8;Q9Y5S8-3
P31930	Cytochrome b-c1 complex subunit 1, mitochondrial (Complex III subunit 1) (Core protein I) (Ubiquinol-cytochrome-c reductase complex core protein 1)	P31930
C9JFR7	Cytochrome c	C9JFR7;P99999

E7ENE7	Cytochrome P450 2D6	E7ENE7;P10635;E9PDB2;G3XAL0;P40926
Q14204	Cytoplasmic dynein 1 heavy chain 1 (Cytoplasmic dynein heavy chain 1) (Dynein heavy chain, cytosolic)	Q14204
E7EQL5	Cytoplasmic dynein 1 intermediate chain 2	Q13409-7;E7EQL5;F8W8S0;Q13409;Q13409-2;Q13409-3;Q13409-5;Q13409-6;E7EV09
H0YCF6	Cytoskeleton-associated protein 5	H0YEK7;Q14008;Q14008-2;Q14008-3;H0YCF6
P28838	Cytosol aminopeptidase (EC 3.4.11.1) (Leucine aminopeptidase 3) (LAP-3) (Leucyl aminopeptidase) (Peptidase S) (Proline aminopeptidase) (EC 3.4.11.5) (Prolyl aminopeptidase)	P28838;P28838-2;H0Y9Q0
B4DUX0	Cytosolic acyl coenzyme A thioester hydrolase (cDNA FLJ60167, highly similar to Cytosolic acyl coenzyme A thioester hydrolase(EC 3.1.2.2))	B4DUX0;O00154;O00154-2;O00154-3;O00154-4;O00154-5;O00154-6;O00154-7;K7EKP8
B7Z382	Cytosolic purine 5'-nucleotidase	B7Z382;P49902;Q5JUV6
P49902	Cytosolic purine 5'-nucleotidase (EC 3.1.3.5) (Cytosolic 5'-nucleotidase II)	P49902-2;P49902;Q5JUV3;Q5JUV4
C9J8U1	Cytospin-A	F8WAN1;P35241;P35241-4;P35241-5;Q69YQ0;Q69YQ0-2;C9J8U1
O43175	D-3-phosphoglycerate dehydrogenase (3-PGDH) (EC 1.1.1.95)	O43175
F6RFD5	Destrin	F6RFD5;P60981;P60981-2
Q9Y295	Developmentally-regulated GTP-binding protein 1 (DRG-1) (Neural precursor cell expressed developmentally down-regulated protein 3) (NEDD-3)	Q9Y295
B4DDD2	Dihydrofolate reductase#	B4DDD2;P00374
F2Z2E3	Dihydrolipoyl dehydrogenase, mitochondrial	P09622-3;F2Z2E3;F8WDM5;P09622
B3KW71	Dihydropteridine reductase	B3KW71;P09417
E9PD68	Dihydropyrimidinase-related protein 1	E9PD68;F5GWI3;H0YBT4;Q14194;Q14194-2;Q14195;Q14195-2;Q16555;Q16555-2
E5RFU4	Dihydropyrimidinase-related protein 2	E5RFU4;E9PD68;Q14194;Q14194-2;Q16555;Q16555-2
Q16555	Dihydropyrimidinase-related protein 2 (DRP-2) (Collapsin response mediator protein 2) (CRMP-2) (N2A3) (Unc-33-like phosphoprotein 2) (ULIP-2)	Q16555;Q16555-2
E7EWB4	Dihydropyrimidinase-related protein 5	E7EWB4;Q9BPU6
G3V180	Dipeptidyl peptidase 3 (HCG2016942, isoform CRA_d)	G3V180;G3V1D3;Q9NY33;Q9NY33-4
B4DTU4	DNA ligase (EC 6.5.1.1)	B4DTU4;F5GZ28;M0R0Q7;P18858;Q2TB12
Q9NRF9	DNA polymerase epsilon subunit 3 (EC 2.7.7.7) (Arsenic-transactivated protein) (AsTP) (Chromatin accessibility complex 17 kDa protein) (CHRA-17) (HuCHRA17) (DNA polymerase II subunit 3) (DNA polymerase epsilon subunit p17)	Q9NRF9
H0Y8E6	DNA replication licensing factor MCM2	H0Y8E6;P49736
P11387	DNA topoisomerase 1 (EC 5.99.1.2) (DNA topoisomerase I)	P11387
E9PCY5	DNA topoisomerase 2 (EC 5.99.1.3)	E9PCY5;P11388;P11388-2;P11388-3;P11388-4;Q02880;Q02880-2

P31689	DnaJ homolog subfamily A member 1 (DnaJ protein homolog 2) (HSDJ) (Heat shock 40 kDa protein 4) (Heat shock protein J2) (HSJ-2) (Human DnaJ protein 2) (hDj-2)	P31689;P31689-2
O60884	DnaJ homolog subfamily A member 2 (Cell cycle progression restoration gene 3 protein) (Dnj3) (Dj3) (HIRA-interacting protein 4) (Renal carcinoma antigen NY-REN-14)	O60884
Q9H3Z4	DnaJ homolog subfamily C member 5 (Cysteine string protein) (CSP)	Q9H3Z4;Q9H3Z4-2
H0Y368	Dolichol-phosphate mannosyltransferase subunit 1	H0Y368;O60762;Q5QPK2
Q9P2X0	Dolichol-phosphate mannosyltransferase subunit 3 (Dolichol-phosphate mannose synthase subunit 3) (DPM synthase subunit 3) (Dolichyl-phosphate beta-D-mannosyltransferase subunit 3) (Mannose-P-dolichol synthase subunit 3) (MPD synthase subunit 3) (Prostin-1)	Q9P2X0;Q9P2X0-2
E7EWT1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit	E7EWT1;P39656;U3KQ84
F8WF32	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	P04843;F8WF32;B7Z4L4
E9PI32	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A (Oligosaccharyl transferase subunit STT3A) (STT3-A) (EC 2.4.99.18) (B5) (Integral membrane protein 1) (Transmembrane protein TMC)	E9PI32;E9PN73;P46977
G5E9C7	Dual-specificity mitogen-activated protein kinase kinase 2 (Mitogen-activated protein kinase kinase 2, isoform CRA_b)	P36507;Q02750;Q02750-2;G5E9C7
Q9UJW0	Dynactin subunit 4 (Dyn4) (Dynactin subunit p62)	E5RGG1;H9KVE0;Q9UJW0;Q9UJW0-2;Q9UJW0-2
G8JLD5	Dynammin-1-like protein	O00429-7;G8JLD5;O00429-8;O00429;O00429-2;O00429-3;O00429-4;O00429-5;O00429-6
F8VRV5	Dynein light chain 1, cytoplasmic	F8VRV5;F8VXL2;P63167
E5RI87	E3 ubiquitin-protein ligase RNF130	E5RI87;Q86XS8-2;Q86XS8;F5H1R4;F5H4A3;K7EM85;K7ES98;Q92619;Q92619-2
F5H012	E3 ubiquitin-protein ligase TRIM21	F5H012;P19474;P19474-2
Q96C19	EF-hand domain-containing protein D2 (Swiprosin-1)	Q96C19
B4DVB8	ELAV-like protein 1 (cD FLJ60076, highly similar to ELAV-like protein 1)	B4DVB8;M0QZR9;M0R055;Q15717
H0YK49	Electron transfer flavoprotein subunit alpha, mitochondrial	H0YK49;H0YNX6;P13804;P13804-2
P38117	Electron transfer flavoprotein subunit beta (Beta-ETF)	M0QY67;P38117;P38117-1
P68104	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor Tu) (EF-Tu) (Eukaryotic elongation factor 1 A-1) (eEF1A-1) (Leukocyte receptor cluster member 7)	P68104;Q05639;Q5VTE0
C9JZW3	Elongation factor 1-beta	C9JZW3;P24534
B4DTG2	Elongation factor 1-gamma#	B4DTG2;P26641

P13639	Elongation factor 2 (EF-2)	P13639
C9IZ01	Elongation factor G, mitochondrial	C9IZ01;Q96RP9;Q96RP9-2
P49411	Elongation factor Tu, mitochondrial (EF-Tu) (P43)	P49411
Q9NZ08	Endoplasmic reticulum aminopeptidase 1 (EC 3.4.11.-) (ARTS-1) (Adipocyte-derived leucine aminopeptidase) (A-LAP) (Aminopeptidase PILS) (Puromycin-insensitive leucyl-specific aminopeptidase) (PILS-AP) (Type 1 tumor necrosis factor receptor shedding aminopeptidase regulator)	Q9NZ08;Q9NZ08-2
Q9BS26	Endoplasmic reticulum resident protein 44 (ER protein 44) (ERp44) (Thioredoxin domain-containing protein 4)	Q9BS26
Q969X5	Endoplasmic reticulum-Golgi intermediate compartment protein 1 (ER-Golgi intermediate compartment 32 kDa protein) (ERGIC-32)	Q969X5;Q969X5-2
P14625	Endoplasmin (94 kDa glucose-regulated protein) (GRP-94) (Heat shock protein 90 kDa beta member 1) (Tumor rejection antigen 1) (gp96 homolog)	P14625
O60869	Endothelial differentiation-related factor 1 (EDF-1) (Multiprotein-bridging factor 1) (MBF1)	O60869;O60869-2;O60869-3
H7C0S6	Engulfment and cell motility protein 1	H7C0S6;Q92556;Q92556-3
G3V279	Enhancer of rudimentary homolog	P84090;G3V279
P30084	Enoyl-CoA hydratase, mitochondrial (EC 4.2.1.17) (Enoyl-CoA hydratase 1) (Short-chain enoyl-CoA hydratase) (SCEH)	P30084
B7Z6Q8	Ephrin type-A receptor 4#	B7Z6Q8;E9PG71;P54764
M0R2A0	ER membrane protein complex subunit 10	M0R2A0;Q5UCC4;Q5UCC4-2
D6R9B1	ETS-related transcription factor Elf-2	D6R9B1
P60842	Eukaryotic initiation factor 4A-I (eIF-4A-I) (eIF4A-I) (EC 3.6.4.13) (ATP-dependent RNA helicase eIF4A-1)	J3KSZ0;J3KT12;J3KTB5;J3KTN0;J3QS69;P60842;P60842-1
E7EQG2	Eukaryotic initiation factor 4A-II	E7EQG2;J3KSZ0;J3KT12;J3KTN0;J3QL43;J3QS69;P38919;P60842;P60842-2;Q14240;Q14240-2;Q9NZE6;J3QL52
H3BR35	Eukaryotic peptide chain release factor GTP-binding subunit ERF3A	H3BR35;P15170;P15170-2;P15170-3;Q8IYD1
B7Z7P8	Eukaryotic peptide chain release factor subunit 1 (cDNA FLJ56175, highly similar to Eukaryotic peptide chain release factor subunit1)	B7Z7P8;I3L492;P62495;Q96CG1
P05198	Eukaryotic translation initiation factor 2 subunit 1 (Eukaryotic translation initiation factor 2 subunit alpha) (eIF-2-alpha) (eIF-2A) (eIF-2alpha)	P05198
P20042	Eukaryotic translation initiation factor 2 subunit 2 (Eukaryotic translation initiation factor 2 subunit beta) (eIF-2-beta)	P20042
P41091	Eukaryotic translation initiation factor 2 subunit 3 (Eukaryotic translation initiation factor 2 subunit gamma X) (eIF-2-gamma X) (eIF-2gX)	P41091;Q2VIR3
F5H335	Eukaryotic translation initiation factor 3 subunit A (eIF3a) (Eukaryotic translation initiation factor 3 subunit 10) (eIF-3-theta)	F5H335;Q14152

P55884	Eukaryotic translation initiation factor 3 subunit B (eIF3b) (Eukaryotic translation initiation factor 3 subunit 9) (Prt1 homolog) (hPrt1) (eIF-3-eta) (eIF3 p110) (eIF3 p116)	P55884;P55884-2
B0QYA4	Eukaryotic translation initiation factor 3 subunit D	B0QYA4;B0QYA5;O15371-2;O15371;O15371-3
E5RGA2	Eukaryotic translation initiation factor 3 subunit E (eIF3e) (Eukaryotic translation initiation factor 3 subunit 6) (eIF-3 p48)	E5RGA2;E5RIT4;H0YBR5;P60228
K7ENA8	Eukaryotic translation initiation factor 3 subunit G	K7ENA8;K7EP16;O75821
Q13347	Eukaryotic translation initiation factor 3 subunit I (eIF3i) (Eukaryotic translation initiation factor 3 subunit 2) (TGF-beta receptor-interacting protein 1) (TRIP-1) (eIF-3-beta) (eIF3 p36)	Q13347
O75822	Eukaryotic translation initiation factor 3 subunit J (eIF3j) (Eukaryotic translation initiation factor 3 subunit 1) (eIF-3-alpha) (eIF3 p35)	O75822-2;O75822-3;O75822
B0QY89	Eukaryotic translation initiation factor 3 subunit L (eIF3l) (Eukaryotic translation initiation factor 3 subunit 6-interacting protein) (Eukaryotic translation initiation factor 3 subunit E-interacting protein)	B0QY89;B0QY90;Q9Y262;Q9Y262-2
B4E2Q4	Eukaryotic translation initiation factor 3 subunit M (cDNA FLJ54904, highly similar to Homo sapiens dendritic cell protein (hfl-B5), mRNA)	B4E2Q4;Q7L2H7;H0YCCQ8
E7EUU4	Eukaryotic translation initiation factor 4 gamma 1	E7EUU4;E7EX73;E9PGM1;Q04637;Q04637-3;Q04637-4;Q04637-5;Q04637-6;Q04637-7;Q04637-8;Q04637-9
I3L397	Eukaryotic translation initiation factor 5A-1	I3L504;P63241;P63241-2;I3L397
C9J4W5	Eukaryotic translation initiation factor 5A-2	C9J4W5;C9J7B5;F8WCJ1;I3L504;P63241;P63241-2;Q9GZV4;I3L397
O43909	Exostosin-like 3 (EC 2.4.1.223) (EXT-related protein 1) (Glucuronyl-galactosyl-proteoglycan 4-alpha-N-acetylglucosaminyltransferase) (Hereditary multiple exostoses gene isolog) (Multiple exostosis-like protein 3) (Putative tumor suppressor protein EXTL3)	O43909;O95502
E7EQR4	Ezrin	E7EQR4;P15311;P26038;P35241;P35241-4;P35241-5
Q9Y5B9	FACT complex subunit SPT16 (Chromatin-specific transcription elongation factor 140 kDa subunit) (FACT 140 kDa subunit) (FACTp140) (Facilitates chromatin transcription complex subunit SPT16) (hSPT16)	Q9Y5B9
C9JUG7	F-actin-capping protein subunit alpha-2 (CapZ alpha-2)	C9JUG7;F8W9N7;P47755;P47755-2
B4DT31	Far upstream element-binding protein 1 (cD FLJ53425, highly similar to Far upstream element-binding protein 1)	Q96AE4;B4DT31;E9PEB5;M0QYG1;M0R0C6;M0R251;M0R263;M0R3J3;Q92945;Q96AE4-2
M0QXW7	Far upstream element-binding protein 2 (FUSE-binding protein 2) (KH type-splicing regulatory protein) (KSRP) (p75)	M0QXW7;M0QYH3;M0R0I5;Q92945
P15090	Fatty acid-binding protein, adipocyte (Adipocyte lipid-binding protein) (ALBP) (Adipocyte-type fatty acid-binding protein) (A-FABP) (AFABP) (Fatty acid-binding protein 4)	P15090

E9PNW8	Fatty acyl-CoA reductase 1	E9PNW8;Q8WVX9
O60907	F-box-like/WD repeat-containing protein TBL1X (SMAP55) (Transducin beta-like protein 1X) (Transducin-beta-like protein 1, X-linked)	O60907;O60907-2;Q9BQ87;Q9BZK7
H0YFT5	Fermitin family homolog 3	H0YFT5;Q86UX7;Q86UX7-2
B1AHL2	Fibulin-1	B1AHL2;P23142-3;F8W7M9;P23142;P23142-2;P23142-4
P21333	Filamin-A (FLN-A) (Actin-binding protein 280) (ABP-280) (Alpha-filamin) (Endothelial actin-binding protein) (Filamin-1) (Non-muscle filamin)	F8WE98;O75369;O75369-2;O75369-3;O75369-4;O75369-5;O75369-6;O75369-8;O75369-9;P21333;P21333-2;Q14315;Q14315-2;Q5HY53
A8MQB8	Fragile X mental retardation protein 1	A8MQB8;G3V0J0;Q06787-9;G8JLE9;Q06787;Q06787-2;Q06787-3;Q06787-4;Q06787-5;Q06787-6;Q06787-7;Q06787-8;Q8IXW7
H3BQN4	Fructose-bisphosphate aldolase (EC 4.1.2.13)	H3BQN4;H3BR68;J3KPS3;P04075;P04075-2
A8MVZ9	Fructose-bisphosphate aldolase C	A8MVZ9;C9J8F3;H3BMQ8;H3BPS8;H3BQN4;H3BR04;H3BU78;H3BUH7;J3KPS3;J3KSV6;J3QKP5;K7EKH5;P04075;P04075-2;P09972
P09382	Galectin-1 (Gal-1) (14 kDa laminin-binding protein) (HLBP14) (14 kDa lectin) (Beta-galactoside-binding lectin L-14-I) (Galaptin) (HBL) (HPL) (Lactose-binding lectin 1) (Lectin galactoside-binding soluble 1) (Putative MAPK-activating protein PM12) (S-Lac lectin 1)	P09382
B7Z2X9	Gamma-enolase (cD FLJ50150, highly similar to Gamma-enolase (EC 4.2.1.11))	B7Z2X9;F5H0C8;F5H1C3;P09104
E9PEV0	Gamma-secretase C-termil fragment 59	E9PEV0;E9PG40;P05067;P05067-10;P05067-11;P05067-4;P05067-6;P05067-8
O60547	GDP-mannose 4,6 dehydratase (EC 4.2.1.47) (GDP-D-mannose dehydratase) (GMD)	O60547;O60547-2
Q8TEQ6	Gem-associated protein 5 (Gemin5)	Q8TEQ6
P13984	General transcription factor IIF subunit 2 (EC 3.6.4.12) (ATP-dependent helicase GTF2F2) (General transcription factor IIF 30 kDa subunit) (Transcription initiation factor IIF subunit beta) (TFIIF-beta) (Transcription initiation factor RAP30)	P13984
G3V4P8	Glia maturation factor beta	G3V4P8;M0QYG8;M0QYJ8;M0R0C1;M0R1D2;O60234;P60983
E7EM57	Glucose-6-phosphate 1-dehydrogenase (EC 1.1.1.49)	E7EM57;E9PD92;P11413;P11413-2;P11413-3;E7EUI8
K7EQ48	Glucose-6-phosphate isomerase (EC 5.3.1.9)	K7EQ48;P06744;P06744-2
K7ELL7	Glucosidase 2 subunit beta	K7ELL7;P14314;P14314-2
B3KV55	Glutamate dehydrogenase 1, mitochondrial#	B3KV55;B4DGN5;P00367;P49448
P00367	Glutamate dehydrogenase 1, mitochondrial (GDH 1) (EC 1.4.1.3)	P00367;P49448
O94925	Glutaminase kidney isoform, mitochondrial (GLS) (EC 3.5.1.2) (K-glutaminase) (L-glutamine amidohydrolase)	O94925;O94925-3
P47897	Glutamine--tRNA ligase (EC 6.1.1.18) (GlutaminyI-tRNA synthetase) (GlnRS)	P47897-2;P47897
O76003	Glutaredoxin-3 (PKC-interacting cousin of thioredoxin) (PICOT) (PKC-theta-interacting	O76003

	protein) (PKCq-interacting protein) (Thioredoxin-like protein 2)	
K7EJ20	Glutathione peroxidase	K7EJ20;K7EKX7;K7ENB4;K7ERP4;P36969;P36969-2;R4GNE4
E9PHN6	Glutathione S-transferase Mu 2	E9PHN6;E9PHN7;E9PLF1;F6XZQ7;P21266;P28161;P28161-2;P46439;Q5T8Q9;Q5T8R1
P78417	Glutathione S-transferase omega-1 (GSTO-1) (EC 2.5.1.18) (Glutathione S-transferase omega 1-1) (GSTO 1-1) (Glutathione-dependent dehydroascorbate reductase) (EC 1.8.5.1) (Monomethylarsonic acid reductase) (MMA(V) reductase) (EC 1.20.4.2) (S-(Phenacyl)glutathione reductase) (SPG-R)	P78417;P78417-2;P78417-3;Q5TA01;Q5TA02
E7EUT5	Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (EC 1.2.1.12) (Peptidyl-cysteine S-nitrosylase GAPDH) (EC 2.6.99.-)	E7EUT5;P04406;P04406-2
F5GYK7	Glycerol-3-phosphate dehydrogenase, mitochondrial	P43304;P43304-2;F5GYK7
P23434	Glycine cleavage system H protein, mitochondrial (Lipoic acid-containing protein)	P23434
P41250	Glycine--tRNA ligase (EC 6.1.1.14) (Diadenosine tetraphosphate synthetase) (AP-4-A synthetase) (Glycyl-tRNA synthetase) (GlyRS)	H7C443;P41249
F2Z349	Glycodelin	Q15431;P14618;F2Z349;H0Y4U4;H0Y6A4;H3BQ34;H3BTN5;P09466;P09466-2;P14618-2;P14618-3;Q504U3;Q5T6T6;Q5VXJ5
B7Z806	Glycogen [starch] synthase, muscle (cD FLJ53681, highly similar to Glycogen (starch) synthase, muscle (EC 2.4.1.11))	B7Z806;F5H1N8;P13807;P13807-2
F5H0U5	Glycolipid transfer protein	F5H0U5;Q9NZD2
B7Z403	Glyoxalase domain-containing protein 4 (cDNA FLJ55095)	B7Z403;I3L3Q4;Q9HC38;Q9HC38-2;Q9HC38-3
H3BM42	Golgi apparatus protein 1 (Golgi apparatus protein 1, isoform CRA_c)	H3BM42;Q92896;Q92896-2;Q92896-3
Q96CN9	GRIP and coiled-coil domain-containing protein 1 (Golgi coiled-coil protein 1)	Q96CN9
B4DJW4	Group XV phospholipase A2 (cDNA FLJ58003, highly similar to 1-O-acylceramide synthase (EC 2.3.1.-))	B4DJW4;H3BM47;H3BMU8;H3BPT3;Q8NCC3
J3KT38	Growth factor receptor-bound protein 2	P62993;J3KT38
P62993	Growth factor receptor-bound protein 2 (Adapter protein GRB2) (Protein Ash) (SH2/SH3 adapter GRB2)	P62993;P62993-2
H0YDZ7	Guanine deaminase	H0YDZ7;J3QSY3;Q5SZC3;Q5SZC6;Q9YT3;Q9Y2T3-2;Q9Y2T3-3
H0YDG2	Guanine nucleotide exchange factor VAV3	H0YDG2;Q9UKW4;Q9UKW4-4
B1AKQ8	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1	F6UT28;P62873;B1AKQ8;P62873-2
C9JIS1	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2	C9JIS1;C9JXA5;C9JZN1;P62879
D6R909	Guanine nucleotide-binding protein subunit beta-2-like 1	D6R909;D6R9L0;D6RAC2;D6RAU2;D6RBD0;D6REE5;D6RFX4;D6RGK8;D6RHH4;E9PD14;P63244;D6R9Z1;D6RFZ9
Q9NY12	H/ACA ribonucleoprotein complex subunit 1 (Nucleolar protein family A member 1) (snoRNP protein GAR1)	Q9NY12;Q9NY12-2

A8MV53	HCG2033702, isoform CRA_a (Suppressor of SWI4 1 homolog)	A8MV53;C9J3W3;Q9NQ55;Q9NQ55-2;Q9NQ55-3
H3BQZ7	HCG2044799 (Protein HNRNPUL2-BSCL2)	H3BQZ7;Q1KMD3
P34931	Heat shock 70 kDa protein 1-like (Heat shock 70 kDa protein 1L) (Heat shock 70 kDa protein 1-Hom) (HSP70-Hom)	P34931
P34932	Heat shock 70 kDa protein 4 (HSP70RY) (Heat shock 70-related protein APG-2)	P34932
B4DY72	Heat shock protein 105 kDa (cD FLJ52360, highly similar to Heat-shock protein 105 kDa)	B4DY72;B4DYH1;Q92598;Q92598-2;Q92598-3
I3L0K7	Heat shock protein 75 kDa, mitochondrial (TNF receptor-associated protein 1, isoform CRA_b)	P07900;P07900-2;P08238;Q86U12;Q12931-2;I3L0K7;I3L239;Q12931;F5H897
P07900	Heat shock protein HSP 90-alpha (Heat shock 86 kDa) (HSP 86) (HSP86) (Lipopolysaccharide-associated protein 2) (LAP-2) (LPS-associated protein 2) (Rel carcinoma antigen NY-REN-38)	G3V2J8;P07900;P07900-2;P08238;Q58FF6;Q58FF7;Q58FF8;Q5T9W8;;Q86U13
E7EVW7	Hematopoietic lineage cell-specific protein (Hematopoietic cell-specific LYN substrate 1) (LckBP1) (p75)	E7EVW7;P14317
F5GWX2	Heme-binding protein 1	F5GWX2;Q9NRV9
P69905	Hemoglobin subunit alpha (Alpha-globin) (Hemoglobin alpha chain)	P69905
E9PBW4	Hemoglobin subunit gamma-2	E9PBW4;P02100;P69891;P69892
A8K8G0	Hepatoma-derived growth factor (cD FLJ75113)	A8K8G0;P51858;P51858-2;P51858-3
P51858	Hepatoma-derived growth factor (HDGF) (High mobility group protein 1-like 2) (HMG-1L2)	P51858
D6R9P3	Heterogeneous nuclear ribonucleoprotein A/B	D6R9P3;D6RBZ0;D6RD18;Q99729-2;Q99729-3;Q99729;Q99729-4
Q13151	Heterogeneous nuclear ribonucleoprotein A0 (hnRNP A0)	Q13151
P51991	Heterogeneous nuclear ribonucleoprotein A3 (hnRNP A3)	P51991;P51991-2
P52597	Heterogeneous nuclear ribonucleoprotein F (hnRNP F) (Nucleolin-like protein mcs94-1) [Cleaved into: Heterogeneous nuclear ribonucleoprotein F, N-termilly processed]	P52597
D6R9T0	Heterogeneous nuclear ribonucleoprotein H	D6RAM1;D6RBM0;D6RDU3;D6RFM3;D6RIH9;D6RIT2;D6RIU0;D6RJ04;E5RGH4;E5RGV0;E7EQJ0;E9PCY7;G8JLB6;H0Yaq2;P31943;P55795;D6R9T0
P61978	Heterogeneous nuclear ribonucleoprotein K (hnRNP K) (Transformation up-regulated nuclear protein) (TUNP)	P61978;P61978-2;P61978-3;Q5T6W5;S4R359
M0QYQ7	Heterogeneous nuclear ribonucleoprotein M	M0QZM1;P52272;P52272-2;M0QYQ7;M0R2T0;M0R019;M0R0N3
F6UXX1	Heterogeneous nuclear ribonucleoprotein Q	F6UXX1;O60506;O60506-2;O60506-3;O60506-4
O60506	Heterogeneous nuclear ribonucleoprotein Q (hnRNP Q) (Glycine- and tyrosine-rich RNA-binding protein) (GRY-RBP) (NS1-associated protein 1) (Synaptotagmin-binding, cytoplasmic RNA-interacting protein)	O60506;O60506-2;O60506-3;O60506-4;O60506-5
B4DT28	Heterogeneous nuclear ribonucleoprotein R (Heterogeneous nuclear ribonucleoprotein R,	B4DT28;O43390;O43390-2;O43390-3;O43390-4

	isoform CRA_a) (cDNA FLJ54544, highly similar to Heterogeneous nuclear ribonucleoprotein R)	
B4DSU6	Heterogeneous nuclear ribonucleoproteins C1/C2 (cDNA FLJ52975, highly similar to Heterogeneous nuclear ribonucleoproteins C)	B4DSU6;B4DY08;G3V251;G3V2Q1;G3V3K6;G3V4C1;G3V4W0;G3V555;G3V575;G3V576;G3V5X6;O60812;P07910;P07910-2;P07910-4
E7ENR4	Hexokinase-1	E7ENR4;P19367;P19367-2;P19367-3;P19367-4
E9PB90	Hexokinase-2 (EC 2.7.1.1) (Hexokinase type II) (HK II) (Muscle form hexokinase)	E9PB90;P52789
P09429	High mobility group protein B1 (High mobility group protein 1) (HMG-1)	P09429;Q5T7C4;Q5T7C6
E7EQU1	High mobility group protein B3	E7EQU1;E7ES08;E9PES6;O15347
F5H2A4	High mobility group protein HMGI-C	F5H2A4;F5H2U8;P52926
F8VNX0	Histidine ammonia-lyase	P42357;F8VNX0;F8W0V1;P42357-2;P42357-3
D6RC06	Histidine triad nucleotide-binding protein 1	D6RC06;D6RD60;D6RE99;D6REP8;P49773
B3KWE1	Histidine--tR ligase, cytoplasmic (Histidyl-tR synthetase, isoform CRA_a) (cD FLJ42841 fis, clone BRCOC2003213, highly similar to Histidyl-tR synthetase (EC 6.1.1.21))	B3KWE1;B4DDD8;B4E1C5;C9JWK3;E7ETE2;P12081;P12081-2;P12081-3;P12081-4
B3KWE1	Histidine--tRNA ligase, cytoplasmic (Histidyl-tRNA synthetase, isoform CRA_a) (cDNA FLJ42841 fis, clone BRCOC2003213, highly similar to Histidyl-tRNA synthetase (EC 6.1.1.21))	B3KWE1;B4DDD8;B4E1C5;P12081;P12081-2;P12081-3;P12081-4
B3KRS5	Histone deacetylase (EC 3.5.1.98)	B3KRS5;E5RFI6;E5RFP9;E5RG37;E5RGV4;E5RH52;E5RHE7;E5RJ04;H3BM24;J3KPW7;Q13547;Q5TEE2;Q92769
Q13547	Histone deacetylase 1 (HD1) (EC 3.5.1.98)	Q13547;Q5TEE2
O75446	Histone deacetylase complex subunit SAP30 (30 kDa Sin3-associated polypeptide) (Sin3 corepressor complex subunit SAP30) (Sin3-associated polypeptide p30)	O75446
P07305	Histone H1.0 (Histone H1') (Histone H1(0)) [Cleaved into: Histone H1.0, N-terminally processed]	P07305
P10412	Histone H1.4 (Histone H1b) (Histone H1s-4)	P10412;P16402;P16403;P22492;Q02539
P16401	Histone H1.5 (Histone H1a) (Histone H1b) (Histone H1s-3)	P16401;Q9UPA5
B4DEB1	Histone H3	B4DEB1;K7EK07;K7EMV3;K7EP01;K7ES00;P68431;P84243;Q16695;Q6NXT2;Q71DI3
P68431	Histone H3.1 (Histone H3/a) (Histone H3/b) (Histone H3/c) (Histone H3/d) (Histone H3/f) (Histone H3/h) (Histone H3/i) (Histone H3/j) (Histone H3/k) (Histone H3/l)	P68431;Q16695;Q5TEC6;Q71DI3
P62805	Histone H4	P62805
E9PC52	Histone-binding protein RBBP7	E9PC52;Q16576;Q16576-2;Q5JP01
C9JAJ9	Histone-binding protein RBBP7	C9JAJ9;E9PC52;E9PIC4;E9PNS2;E9PNS6;Q09028;Q09028-2;Q09028-3;Q16576;Q16576-2
Q6NXR6	Histone-lysine N-methyltransferase setd3 (SETD3 protein)	Q6NXR6;Q86TU7;Q86TU7-2;Q86TU7-3
B7Z5N8	Homeobox protein Hox-B3 (cDNA FLJ51054,	B7Z5N8;B7ZAD0;F8VXG0;O43365;P14651;P31249

	highly similar to Homeobox protein Hox-B3)	
F8WAQ7	Hsc70-interacting protein (Hip) (Aging-associated protein 2) (Progesterone receptor-associated p48 protein) (Protein FAM10A1) (Putative tumor suppressor ST13) (Renal carcinoma antigen NY-REN-33) (Suppression of tumorigenicity 13 protein)	F8WAQ7;P50502;Q8NFI4;F6VDH7;H7C3I1
Q01581	Hydroxymethylglutaryl-CoA synthase, cytoplasmic (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl coenzyme A synthase)	Q01581
P00492	Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) (HGPRTase) (EC 2.4.2.8)	P00492
B7Z909	Hypoxia up-regulated protein 1#	B7Z909;E9PJ21;E9PL22;Q9Y4L1
B1P7G3	ICSU (ISCU)	B1P7G3;B3KQ30;B4DNC9;F5H5N2;Q9H1K1;Q9H1K1-2
P01876	Ig alpha-1 chain C region	P01876;P01877
P01857	Ig gamma-1 chain C region	P01857
P01859	Ig gamma-2 chain C region	P01859
P01765	Ig heavy chain V-III region TIL	P01765;P01774;P01776;P01779
P01764	Ig heavy chain V-III region VH26	P01764
P01834	Ig kappa chain C region	P01834
P01596	Ig kappa chain V-I region CAR	P01596;P01598
P80748	Ig lambda chain V-III region LOI	P80748
P01714	Ig lambda chain V-III region SH	P01714
A0M8Q6	Ig lambda-7 chain C region	A0M8Q6;B9A064;P0CG04
O00629	Importin subunit alpha-3 (Importin alpha Q1) (Qip1) (Karyopherin subunit alpha-4)	O00629
O95373	Importin-7 (Imp7) (Ran-binding protein 7) (RanBP7)	O95373
E7ETK5	Inosine-5'-monophosphate dehydrogenase 2	E7ETK5;H0Y4R1;P12268
E5RG13	Inositol monophosphatase 1	E5RG13;H0YBL1;P29218;P29218-3;E5RI P7
O00425	Insulin-like growth factor 2 mRNA-binding protein 3 (IGF2 mRNA-binding protein 3) (IMP-3) (IGF-II mRNA-binding protein 3) (KH domain-containing protein overexpressed in cancer) (hKOC) (VICKZ family member 3)	O00425;Q9NZI8
Q9Y287	Integral membrane protein 2B (Immature BRI2) (imBRI2) (Protein E25B) (Transmembrane protein BRI) (Bri) [Cleaved into: BRI2, membrane form (Mature BRI2) (mBRI2); BRI2 intracellular domain (BRI2 ICD); BRI2C, soluble form; Bri23 peptide (Bri2-23) (ABri23) (C-terminal peptide) (P23 peptide)]	Q9Y287-2;Q9Y287;U3KQL7
A8MYE6	Integrin beta	A8MYE6;P05107
H7C4N8	Integrin beta-1	H7C4N8;P05556;P05556-2;P05556-3;P05556-4;P05556-5
H0YG72	Integrin-alpha FG-GAP repeat-containing protein 2	H0YG72
Q9BYX4	Interferon-induced helicase C domain-containing protein 1 (EC 3.6.4.13) (Clinically amyopathic	Q9BYX4

	dermatomyositis autoantigen 140 kDa) (CADM-140 autoantigen) (Helicase with 2 CARD domains) (Helicard) (Interferon-induced with helicase C domain protein 1) (Melanoma differentiation-associated protein 5) (MDA-5) (Murabutide down-regulated protein) (RIG-I-like receptor 2) (RLR-2) (RNA helicase-DEAD box protein 116)	
Q12906	Interleukin enhancer-binding factor 3 (Double-stranded R-binding protein 76) (DRBP76) (M-phase phosphoprotein 4) (MPP4) (Nuclear factor associated with dsR) (NFAR) (Nuclear factor of activated T-cells 90 kDa) (NF-AT-90) (Translatiol control protein 80) (TCP80)	Q12906;Q12906-2;Q12906-3;Q12906-4;Q12906-5;Q12906-6;Q12906-7
Q9H1K1	Iron-sulfur cluster assembly enzyme ISCU, mitochondrial (NifU-like N-terminal domain-containing protein) (NifU-like protein)	Q9H1K1;Q9H1K1-2
C9JE02	Isoamyl acetate-hydrolyzing esterase 1 homolog	C9JE02;H7C5G1;Q2TAA2
O43837	Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial (EC 1.1.1.41) (Isocitric dehydrogenase subunit beta) (NAD(+)-specific ICDH subunit beta)	O43837;O43837-3;O43837-2
B4DFL2	Isocitrate dehydrogenase [NADP], mitochondrial#	B4DFL2;B4DSZ6;H0YL11;P48735
H0YKD0	Isocitrate dehydrogenase [D] subunit alpha, mitochondrial	H0YKD0;H0YL72;H0YLI6;H0YM64;H0YNF8;P50213
J3KR24	Isoleucine--tR ligase, cytoplasmic (Isoleucine-tR synthetase, isoform CRA_d)	J3KR24;P41252;Q5TCC4
Q13907	Isopentenyl-diphosphate Delta-isomerase 1 (EC 5.3.3.2) (Isopentenyl pyrophosphate isomerase 1) (IPP isomerase 1) (IPPI1)	Q13907;Q13907-2
H0YLC3	Isovaleryl-CoA dehydrogenase, mitochondrial	H0YLC3;P26440;P26440-2
P33176	Kinesin-1 heavy chain (Conventional kinesin heavy chain) (Ubiquitous kinesin heavy chain) (UKHC)	P33176
Q04760	Lactoylglutathione lyase (EC 4.4.1.5) (Aldoketomutase) (Glyoxalase I) (Glx I) (Ketone-aldehyde mutase) (Methylglyoxalase) (S-D-lactoylglutathione methylglyoxal lyase)	Q04760;Q04760-2
A2T926	Lamina-associated polypeptide 2, isoforms beta/gamma#	A2T926;G5E972;H0YJH7;P42166;P42167;P42167-2
C9JES9	Lamin-B receptor	C9JES9;C9JXK0;Q14739
P20700	Lamin-B1	P20700
E5RH50	La-related protein 1	Q6PKG0;Q6PKG0-3;E5RH50
F8VNV1	La-related protein 4	F8VY40;F8W1Z5;Q71RC2;Q71RC2-2;Q71RC2-3;Q71RC2-4;Q71RC2-5;Q71RC2-6;Q71RC2-7;F8VNV1
Q96AG4	Leucine-rich repeat-containing protein 59 (Ribosome-binding protein p34) (p34)	Q96AG4
B4DEH5	Leukotriene A-4 hydrolase (cDNA FLJ51712, moderately similar to Leukotriene A-4 hydrolase (EC 3.3.2.6))	B4DEH5;P09960;P09960-2;P09960-3;P09960-4
F6S2S5	LIM and SH3 domain protein 1	F6S2S5;K7ESD6;Q14847;Q14847-2;Q14847-3;C9J9W2

F5H5G1	Limbic system-associated membrane protein	C9J5G3;F5H5G1;H3BLU2;Q13448
I3L1H3	Lipopolysaccharide-induced tumor necrosis factor-alpha factor	I3L1H3;Q99732
P06858	Lipoprotein lipase (LPL) (EC 3.1.1.34)	P06858
A8MW50	L-lactate dehydrogenase (EC 1.1.1.27)	A8MW50;F5H155;F5H245;F5H5G7;G3XAP5;P00338;P00338-2;P00338-3;P00338-4;P00338-5;P07195;P07864;Q6ZMR3
P00338	L-lactate dehydrogenase A chain (LDH-A) (EC 1.1.1.27) (Cell proliferation-inducing gene 19 protein) (LDH muscle subunit) (LDH-M) (Renal carcinoma antigen NY-REN-59)	P00338;P00338-3;P00338-4
K7EJE8	Lon protease homolog, mitochondrial (EC 3.4.21.-) (Lon protease-like protein) (Mitochondrial ATP-dependent protease Lon) (Serine protease 15)	P36776-3;K7EJE8;K7EKE6;K7ER27;P36776;P36776-2
O60488	Long-chain-fatty-acid--CoA ligase 4 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 4) (LACS 4)	O60488;O60488-2
A8MYV2	LUC7-like (S. cerevisiae) (LUC7-like (S. cerevisiae), isoform CRA_f) (Putative RNA-binding protein Luc7-like 1)	A8MYV2;B8ZZ10;Q96HJ9-2;Q9NQ29;Q9NQ29-2;Q9NQ29-3;Q9Y383;Q9Y383-2;Q9Y383-3
P05455	Lupus La protein (La autoantigen) (La ribonucleoprotein) (Sjogren syndrome type B antigen) (SS-B)	P05455
F8W6P5	LVV-hemorphin-7	F8W6P5;P68871
O94772	Lymphocyte antigen 6H (Ly-6H)	O94772;O94772-2
B1ALG6	Lymphoid-specific helicase	B1ALG6;Q9NRZ9;Q9NRZ9-2;Q9NRZ9-3;Q9NRZ9-4;Q9NRZ9-5;Q9NRZ9-6;Q9NRZ9-7;Q9NRZ9-8
Q9HD34	LYR motif-containing protein 4	Q9HD34
H3BPV7	Lysine--tRNA ligase	H3BPV7;H3BVA8;J3KRL2;Q15046;Q15046-2
B4DWL3	Lysosome-associated membrane glycoprotein 1#	B4DWL3;P11279
F8VV32	Lysozyme C	F8VV32;P61626
P40121	Macrophage-capping protein (Actin regulatory protein CAP-G)	B8ZZL6;E7ENU9;P40121;P40121-1
A2A2V1	Major prion protein	A2A2V1;P04156;P04156-2
G3XAL0	Malate dehydrogenase (EC 1.1.1.37)	B9A041;C9JF79;P40925;P40925-2;P40925-3;C9JRL3
F5GX14	Malectin	F5H1S8;H0YG07;Q14165
Q9ULC4	Malignant T-cell-amplified sequence 1 (MCT-1) (Multiple copies T-cell malignancies)	Q9ULC4;Q9ULC4-2;Q9ULC4-3
B7Z1L3	Membrane-associated progesterone receptor component 1	O15173;O15173-2;B7Z1L3;O00264
P55145	Mesencephalic astrocyte-derived neurotrophic factor (Arginine-rich protein) (Protein ARMET)	P55145
P02795	Metallothionein-2 (MT-2) (Metallothionein-2A) (Metallothionein-II) (MT-II)	P02795;P04732;P13640;P13640-2;P80297;Q8N339
O94776	Metastasis-associated protein MTA2 (Metastasis-associated 1-like 1) (MTA1-L1 protein) (p53 target protein in deacetylase complex)	O94776
Q13505	Metaxin-1 (Mitochondrial outer membrane import complex protein 1)	Q13505;Q13505-2;Q13505-3
A6NC17	Methionine--tR ligase, cytoplasmic	A6NC17;P56192

P22033	Methylmalonyl-CoA mutase, mitochondrial (MCM) (EC 5.4.99.2) (Methylmalonyl-CoA isomerase)	P22033
K7EM59	Methylthioribose-1-phosphate isomerase	Q9BV20;K7EM59
A6NCE7	Microtubule-associated proteins 1A/1B light chain 3 beta 2 (Microtubule-associated proteins 1A/1B light chain 3B-like)	A6NCE7;H3BTL1;Q9GZQ8
Q9Y3D6	Mitochondrial fission 1 protein (FIS1 homolog) (hFis1) (Tetratricopeptide repeat protein 11) (TPR repeat protein 11)	Q9Y3D6
K7EIT2	Mitochondrial import inner membrane translocase subunit Tim13 (Translocase of inner mitochondrial membrane 13 homolog (Yeast), isoform CRA_b)	K7EIT2;Q9Y5L4
Q9NS69	Mitochondrial import receptor subunit TOM22 homolog (hTom22) (1C9-2) (Translocase of outer membrane 22 kDa subunit homolog)	Q9NS69
O94826	Mitochondrial import receptor subunit TOM70 (Mitochondrial precursor proteins import receptor) (Translocase of outer membrane 70 kDa subunit)	O94826
B9A067	Mitochondrial inner membrane protein	B9A067;C9J406;H7C463;Q16891;Q16891-2;Q16891-3;Q16891-4
P28482	Mitogen-activated protein kinase 1 (MAP kinase 1) (MAPK 1) (EC 2.7.11.24) (ERT1) (Extracellular signal-regulated kinase 2) (ERK-2) (MAP kinase isoform p42) (p42-MAPK) (Mitogen-activated protein kinase 2) (MAP kinase 2) (MAPK 2)	P28482;P28482-2
Q9UKD2	mRNA turnover protein 4 homolog	Q9UKD2
H0YDS7	MutS protein homolog 5	H0YDS7
O00499	Myc box-dependent-interacting protein 1 (Amphiphysin II) (Amphiphysin-like protein) (Box-dependent myc-interacting protein 1) (Bridging integrator 1)	O00499-10;O00499-11;O00499-2;O00499-4;O00499-6;O00499-7;O00499-8;O00499-9
P02689	Myelin P2 protein (Peripheral myelin protein 2)	P02689;P05413;S4R371;S4R3A2
J3QRS3	Myosin regulatory light chain 12A (Myosin regulatory light chain MRCL3, isoform CRA_b)	J3QRS3;O14950;P19105
F8W6L6	Myosin-10	F8W6L6;P35579;P35579-2;P35580;P35580-2;P35580-3;P35580-4;P35749;P35749-2;P35749-3;P35749-4;P35580-5
F2Z2U8	Myosin-14	F2Z2U8;G8JLL9;P35579;P35749;P35749-2;P35749-3;P35749-4;Q7Z406;Q7Z406-2;Q7Z406-4;Q7Z406-5;Q7Z406-6
P35579	Myosin-9 (Cellular myosin heavy chain, type A) (Myosin heavy chain 9) (Myosin heavy chain, non-muscle IIa) (Non-muscle myosin heavy chain A) (NMMHC-A) (Non-muscle myosin heavy chain IIa) (NMMHC II-a) (NMMHC-IIA)	P35579;B1AH99;Q5BKV1
B4DGT0	N(G),N(G)-dimethylarginine dimethylaminohydrolase 1 (cDNA FLJ54083, highly similar to NG,NG-dimethylarginine dimethylaminohydrolase 1 (EC 3.5.3.18))	B4DGT0;B4DYP1;O94760;O94760-2
O43505	N-acetyllactosaminide beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.149)	O43505

	(l-beta-1,3-N-acetylglucosaminyltransferase) (iGnT) (Poly-N-acetyllactosamine extension enzyme) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 1)	
Q9H0A0	N-acetyltransferase 10 (EC 2.3.1.-)	Q9H0A0-2;Q9H0A0
A8MZB2	N-acetyltransferase 5 (ARD1 homolog, S. cerevisiae), isoform CRA_a (N-alpha-acetyltransferase 20)	A8MZB2;P61599;P61599-2
A6NKZ2	N-acylglucosamine 2-epimerase	A6NKZ2;P51606
Q8NFW8	N-acylneuraminate cytidyltransferase (EC 2.7.7.43) (CMP-N-acetylneuraminic acid synthase) (CMP-NeuNAc synthase)	Q8NFW8
P23368	NAD-dependent malic enzyme, mitochondrial (NAD-ME) (EC 1.1.1.38) (Malic enzyme 2)	P23368;P23368-2
E7EMD0	NADPH--cytochrome P450 reductase	E7EMD0;E7EPN3;E7EY7;F5H468;H0Y4R2;P16435
Q9BXJ9	N-alpha-acetyltransferase 15, NatA auxiliary subunit (Gastric cancer antigen Ga19) (N-terminal acetyltransferase) (NMDA receptor-regulated protein 1) (Protein tubedown-1) (Tbdn100)	Q9BXJ9;Q9BXJ9-4
B0AZT5	N-alpha-acetyltransferase 50 (cDNA FLJ51877, highly similar to Homo sapiens Mak3 homolog (MAK3), mRNA) (cDNA, FLJ79525, highly similar to Homo sapiens Mak3 homolog (MAK3), mRNA)	B0AZT5;C9J5D1;E7EQ69;Q9GZZ1;Q9GZZ1-2
B1AKJ5	Nardilysin (Nardilysin (N-arginine dibasic convertase), isoform CRA_d)	B1AKJ5;F5H7V1;G3V1R5;O43847;O43847-2
E9PAV3	Nascent polypeptide-associated complex subunit alpha, muscle-specific form (Alpha-NAC, muscle-specific form) (skNAC)	E9PAV3;E9PAV3-2;F8VNW4;F8VZ58;F8VZJ2;F8W0W4;F8W1N5;H0YHX9;Q13765
F8W050	Nck-associated protein 1-like	F8W050;P55160;P55160-2
H7BYX6	Neural cell adhesion molecule 1	H7BYX6;P13591;P13591-1;P13591-3;P13591-4;P13591-5;R4GMN9;S4R389;S4R3Z6
H9KV31	Neural cell adhesion molecule 2	H9KV31;O15394
O00533	Neural cell adhesion molecule L1-like protein (Close homolog of L1) [Cleaved into: Processed neural cell adhesion molecule L1-like protein]	C9J905;C9JW79;O00533;O00533-2;C9JH36
E7ERL8	Neurexin-1-beta	E7ERL8;F5GYC7;F8WB18;Q9ULB1;Q9ULB1-2;Q9ULB1-3;H0YJL2;Q9Y4C0;Q9Y4C0-4
Q9Y4C0	Neurexin-3 (Neurexin III-alpha) (Neurexin-3-alpha)	Q9Y4C0;Q9Y4C0-4
Q9HDB5	Neurexin-3-beta (Neurexin III-beta) [Cleaved into: Neurexin-3-beta, soluble form; Neurexin-3-beta, C-terminal fragment (NRXN3-CTF)]	Q9HDB5;Q9HDB5-2;Q9HDB5-3;Q9HDB5-4;Q9Y4C0;Q9Y4C0-3;Q9Y4C0-4
Q09666	Neuroblast differentiation-associated protein AHNAK (Desmoyokin)	Q09666
P29120	Neuroendocrine convertase 1 (NEC 1) (EC 3.4.21.93) (Prohormone convertase 1) (Proprotein convertase 1) (PC1)	P29120;P29120-2
D6RBU5	Neurofascin	D6RBU5;F8W791;F8W792;F8W8X7;F8W9B6;F8WAT1;H7BY57;J3QXSX2;O94856;O94856-10;O94856-11;O94856-12;O94856-1

		3;O94856-2;O94856-3;O94856-4;O94856-5;O94856-6;O94856-7;O94856-8;O94856-9;X6RKN2
O95502	Neuronal pentraxin receptor	O95502
Q15818	Neuronal pentraxin-1 (NP1) (Neuronal pentraxin I) (NP-I)	Q15818
Q5BLP8	Neuropeptide-like protein C4orf48	Q5BLP8;Q5BLP8-2;X6RBU3
B7Z1I4	Neurotrimin (cDNA FLJ57258, highly similar to Neurotrimin)	B7Z1I4;B7Z1Z5;F8VTR5;Q9P121;Q9P121-2;Q9P121-3;Q9P121-4
E9PKU7	Neutral alpha-glucosidase AB	E9PKU7;F5H6X6;Q14697;Q14697-2
Q96TA1	Niban-like protein 1 (Meg-3) (Melanoma invasion by ERK) (MINERVA) (Protein FAM129B)	Q96TA1;Q96TA1-2
P35228	Nitric oxide synthase, inducible (EC 1.14.13.39) (Hepatocyte NOS) (HEP-NOS) (Inducible NO synthase) (Inducible NOS) (iNOS) (NOS type II) (Peptidyl-cysteine S-nitrosylase NOS2)	P35228;P35228-2
J3KN36	Nodal modulator 3	J3KN36;P69849;Q15155;Q5JPE7;Q5JPE7-2
P05204	Non-histone chromosomal protein HMG-17 (High mobility group nucleosome-binding domain-containing protein 2)	P05204
Q9Y266	Nuclear migration protein nudC (Nuclear distribution protein C homolog)	Q9Y266
Q12769	Nuclear pore complex protein Nup160 (160 kDa nucleoporin) (Nucleoporin Nup160)	Q12769
H3BPA9	Nuclear pore complex protein Nup93	H3BVG0;Q8N1F7;Q8N1F7-2;H3BPA9
H3BRV9	Nuclear transport factor 2	H3BRV9;P61970
Q02818	Nucleobindin-1 (CALNUC)	H7BZI1;Q02818
B7Z7A3	Nucleolar GTP-binding protein 1#	B7Z7A3;Q5T3R7;Q9BZE4
H0YDU4	Nucleolar protein 56	H0YDU4;O00567;Q5JXT2
H7BZ72	Nucleolar protein 58	H7BZ72;Q9Y2X3
Q9NR30	Nucleolar RNA helicase 2 (EC 3.6.4.13) (DEAD box protein 21) (Gu-alpha) (Nucleolar RNA helicase Gu) (Nucleolar RNA helicase II) (RH II/Gu)	Q9NR30;Q9NR30-2
E9PKP7	Nucleolar transcription factor 1	E9PKP7;P17480;P17480-2
P19338	Nucleolin (Protein C23)	P19338
H7BYF2	Nucleoporin p58/p45	H7BYF2;Q5JRG1;Q9BVL2;Q9BVL2-2;Q9BVL2-3
P12270	Nucleoprotein TPR (Megator) (NPC-associated intranuclear protein) (Translocated promoter region protein)	P12270
E7ERL0	Nucleoside diphosphate kinase A	E7ERL0;F6XY72;J3KPD9;O60361;P15531;P15531-2;P22392;P22392-2;Q32Q12;C9K028
B3KNT8	Nucleosome assembly protein 1-like 1	B3KNT8;B7Z9C2;F5H4R6;F8VRJ2;F8VV59;F8VVB5;F8VY35;F8W020;F8W0J6;F8W118;F8W543;H0YH88;H0YHC3;H0YIV4;P55209
C9JZI7	Nucleosome assembly protein 1-like 4	C9JZI7;H0YCI4;Q99733;Q99733-2
E5RFP0	NudC domain-containing protein 2	E5RFP0;Q8WVJ2
Q14982	Opioid-binding protein/cell adhesion molecule (OBCAM) (OPCML) (Opioid-binding cell adhesion molecule) (IgLON family member 1)	Q14982-4;Q14982;Q14982-2;Q14982-3

Q92882	Osteoclast-stimulating factor 1	Q92882
D6R9C5	Osteopontin	D6R9C5;P10451;P10451-2;P10451-3;P10451-4;P10451-5
B1AKJ6	Oxysterol-binding protein	B1AKJ6;E9PJW9;J3KPA3;Q96SU4;Q96SU4-2;Q96SU4-3;Q96SU4-4;Q96SU4-5;Q96SU4-6;Q96SU4-7
P19021	Peptidyl-glycine alpha-amidating monooxygenase (PAM) [Includes: Peptidylglycine alpha-hydroxylating monooxygenase (PHM) (EC 1.14.17.3); Peptidyl-alpha-hydroxyglycine alpha-amidating lyase (EC 4.3.2.5) (Peptidylamidoglycolate lyase) (PAL)]	P19021;P19021-2;P19021-3;P19021-4;P19021-5;P19021-6
A2BFH1	Peptidyl-prolyl cis-trans isomerase A-like 4G (PPlase A-like 4G) (EC 5.2.1.8) (Peptidylprolyl cis-trans isomerase A-like 4)	A2BFH1;C9J5S7;F5H284;F8WE65;P62937;Q9Y536
H0Y8J0	Peptidyl-prolyl cis-trans isomerase D (PPlase D) (EC 5.2.1.8) (40 kDa peptidyl-prolyl cis-trans isomerase) (Cyclophilin-40) (CYP-40) (Cyclophilin-related protein) (Rotamase D)	Q08752;H0Y8J0
P30405	Peptidyl-prolyl cis-trans isomerase F, mitochondrial (PPlase F) (EC 5.2.1.8) (Cyclophilin D) (CyP-D) (CypD) (Cyclophilin F) (Mitochondrial cyclophilin) (CyP-M) (Rotamase F)	P30405
P62942	Peptidyl-prolyl cis-trans isomerase FKBP1A (PPlase FKBP1A) (EC 5.2.1.8) (12 kDa FK506-binding protein) (12 kDa FKBP) (FKBP-12) (Calstabin-1) (FK506-binding protein 1A) (FKBP-1A) (Immunophilin FKBP12) (Rotamase)	P62942
P26885	Peptidyl-prolyl cis-trans isomerase FKBP2 (PPlase FKBP2) (EC 5.2.1.8) (13 kDa FK506-binding protein) (13 kDa FKBP) (FKBP-13) (FK506-binding protein 2) (FKBP-2) (Immunophilin FKBP13) (Rotamase)	P26885
G3V5F2	Peptidyl-prolyl cis-trans isomerase FKBP3	G3V5F2;Q00688
K7EN45	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	K7EN45;Q13526
Q15269	Periodic tryptophan protein 2 homolog	Q15269
P32119	Peroxiredoxin-2 (EC 1.11.1.15) (Natural killer cell-enhancing factor B) (NKEF-B) (PRP) (Thiol-specific antioxidant protein) (TSA) (Thioredoxin peroxidase 1) (Thioredoxin-dependent peroxide reductase 1)	P32119;Q06830
H7C3T4	Peroxiredoxin-4 (EC 1.11.1.15) (Antioxidant enzyme AOE372) (AOE37-2) (Peroxiredoxin IV) (Prx-IV) (Thioredoxin peroxidase A0372) (Thioredoxin-dependent peroxide reductase A0372)	H7C3T4;Q06830;Q13162
P30041	Peroxiredoxin-6 (EC 1.11.1.15) (1-Cys peroxidase) (1-Cys PRX) (24 kDa protein) (Acidic calcium-independent phospholipase A2) (aiPLA2) (EC 3.1.1.-) (Antioxidant protein 2) (Liver 2D page spot 40) (Non-selenium glutathione peroxidase) (NSGPx) (EC 1.11.1.9) (Red blood cells page spot 12)	P30041

Q8WW12	PEST proteolytic signal-containing nuclear protein (PCNP) (PEST-containing nuclear protein)	Q8WW12;Q8WW12-2
Q7RTV0	PHD finger-like domain-containing protein 5A (PHD finger-like domain protein 5A) (Splicing factor 3B-associated 14 kDa protein) (SF3b14b)	Q7RTV0
F8VVM2	Phosphate carrier protein, mitochondrial	F8VVM2;Q00325;Q00325-2
P30086	Phosphatidylethanolamine-binding protein 1 (PEBP-1) (HCNPpp) (Neuropolypeptide h3) (Prostatic-binding protein) (Raf kinase inhibitor protein) (RKIP) [Cleaved into: Hippocampal cholinergic neurostimulating peptide (HCNP)]	P30086
Q96S96	Phosphatidylethanolamine-binding protein 4 (PEBP-4) (hPEBP4) (Protein cousin-of-RKIP 1)	Q96S96
F5GWE5	Phosphatidylinositol transfer protein alpha isoform	F5GWE5;I3L459;I3L4H1;Q00169
E9PJT1	Phosphatidylinositol-binding clathrin assembly protein	E9PJT1;E9PK13;Q13492;Q13492-2;Q13492-3;Q13492-5
B4DW73	Phosphoenolpyruvate carboxykinase [GTP], mitochondrial (cDNA FLJ50710, highly similar to Phosphoenolpyruvate carboxykinase (GTP), mitochondrial (EC 4.1.1.32)) (cDNA, FLJ79105, highly similar to Phosphoenolpyruvate carboxykinase (GTP), mitochondrial (EC 4.1.1.32))	H0YM31;Q16822;Q16822-2;B4DW73;H0YML5
E7ERH5	Phosphoglycerate kinase 1	E7ERH5;P00558
P15259	Phosphoglycerate mutase 2 (EC 3.1.3.13) (EC 5.4.2.11) (EC 5.4.2.4) (BPG-dependent PGAM 2) (Muscle-specific phosphoglycerate mutase) (Phosphoglycerate mutase isozyme M) (PGAM-M)	P15259;P18669;Q8N0Y7
C9JDH0	Phosphoribosyl pyrophosphate synthase-associated protein 2	C9JDH0;C9JDU5;C9JJS3;C9K0K7;E7EPA1;E7EW35;I3L164;I3L331;O60256;O60256-3
E9PBS1	Phosphoribosylaminoimidazole carboxylase	E9PBS1;P22234;P22234-2
F8WEF0	Phosphoribosylaminoimidazolecarboxamide formyltransferase	C9JLK0;F5GWY2;P31939;P31939-1
Q9Y617	Phosphoserine aminotransferase (EC 2.6.1.52) (Phosphohydroxythreonine aminotransferase) (PSAT)	Q9Y617;Q9Y617-2
I3L4N7	Pigment epithelium-derived factor	I3L4N7;P36955
F5GZA6	PILR alpha-associated neural protein	Q8IYJ0;Q8IYJ0-2;F5GZA6;F5H0N9;F5H191
Q9H307	Pinin (140 kDa nuclear and cell adhesion-related phosphoprotein) (Desmosome-associated protein) (Domain-rich serine protein) (DRS protein) (DRSP) (Melanoma metastasis clone A protein) (Nuclear protein SDK3) (SR-like protein)	Q9H307;Q9H307-2
B4E1F0	Plasma protease C1 inhibitor#	B4E1F0;B4E1H2;E9PGN7;H9KV48;P05155
Q8NC51	Plasminogen activator inhibitor 1 RNA-binding protein (PAI1 RNA-binding protein 1) (PAI-RBP1) (SERPINE1 mRNA-binding protein 1)	Q8NC51;Q8NC51-2;Q8NC51-3;Q8NC51-4
P13796	Plastin-2 (L-plastin) (LC64P) (Lymphocyte cytosolic protein 1) (LCP-1)	P13796
B4DGB4	Plastin-3#	B4DGB4;B4DI60;B7Z6M1;F8W8D8;P1379

		7
P08567	Pleckstrin (Platelet 47 kDa protein) (p47)	P08567
Q15149	Plectin (PCN) (PLTN) (Hemidesmosomal protein 1) (HD1) (Plectin-1)	Q15149;Q15149-2;Q15149-3;Q15149-4;Q15149-5;Q15149-6;Q15149-7;Q15149-8;Q15149-9
Q15365	Poly(rC)-binding protein 1 (Alpha-CP1) (Heterogeneous nuclear ribonucleoprotein E1) (hnRNP E1) (Nucleic acid-binding protein SUB2.3)	Q15365
E7EQV3	Polyadenylate-binding protein 1	E7EQV3;E7ERJ7;H0YAS6;H0YAS7;H0YB75;H0YC10;P11940;P11940-2;Q9H361
B4DEH8	Polyadenylate-binding protein 2 (cDNA FLJ57714, highly similar to Poly(A)-binding protein 2)	B4DEH8;G3V4T2;H0YJH9;Q86U42;Q86U42-2;Q92843-2
C9J2C3	Polypeptide N-acetylgalactosaminyltransferase 3	C9J2C3;Q14435;Q14435-2;Q8NCL4;S4R3S5
K7EKJ7	Polypyrimidine tract-binding protein 1	K7EKJ7;K7ELW5;K7ES59;P26599;P26599-2;P26599-3
A5A3E0	POTE ankyrin domain family member F (ANKRD26-like family C member 1B) (Chimeric POTE-actin protein)	A5A3E0;I3L1U9;P0CG38;P0CG39;P60709;P62736;P63261;P63267;P63267-2;P68032;P68133;Q562R1;Q5T8M7;Q6S8J3;Q9BYX7;I3L4N8;F5H6T1;P61160;P61160-2;B4DXP9;F5H3I4;P61163;R4GMT0
E5RGS4	Prefoldin subunit 1	E5RGS4;O60925
Q9UHV9	Prefoldin subunit 2	Q9UHV9
F5H2A7	Prefoldin subunit 3	F5H2A7;P61758
A2AB88	Prefoldin subunit 6	A2AB88;O15212
P02545	Prelamin-A/C [Cleaved into: Lamin-A/C (70 kDa lamin) (Renal carcinoma antigen NY-REN-32)]	H0YAB0;P02545;P02545-2;P02545-3;P02545-4;P02545-5;P02545-6;Q5TCI9
O75400	Pre-mRNA-processing factor 40 homolog A (Fas ligand-associated factor 1) (Formin-binding protein 11) (Formin-binding protein 3) (Huntingtin yeast partner A) (Huntingtin-interacting protein 10) (HIP-10) (Huntingtin-interacting protein A) (Renal carcinoma antigen NY-REN-6)	O75400;O75400-2;O75400-3
I3L3Z8	Pre-mRNA-processing-splicing factor 8	I3L3Z8;Q6P2Q9
Q92620	Pre-mRNA-splicing factor ATP-dependent RNA helicase PRP16 (EC 3.6.4.13) (ATP-dependent RNA helicase DHX38) (DEAH box protein 38)	Q92620
Q8IY81	pre-rRNA processing protein FTSJ3 (EC 2.1.1.-) (2'-O-ribose RNA methyltransferase SPB1 homolog) (Protein ftsJ homolog 3) (Putative rRNA methyltransferase 3)	Q8IY81
Q5JRX3	Presequence protease, mitochondrial (hPreP) (EC 3.4.24.-) (Pitriysin metalloproteinase 1) (Metalloprotease 1) (hMP1)	Q5JRX3;Q5JRX3-2;Q5JRX3-3
C9JMU5	Probable ATP-dependent R helicase DDX17	C9JMU5;H3BLZ8;Q92841;Q92841-1;Q92841-2;Q92841-3
B4DLW8	Probable ATP-dependent R helicase DDX5 (cD FLJ59339, highly similar to Probable ATP-dependent R helicase DDX5 (EC 3.6.1.-))	B4DLW8;J3KRX8;J3KTA4;J3QKN9;J3QR02;J3QRQ7;P17844
Q9BUQ8	Probable ATP-dependent RNA helicase DDX23 (EC 3.6.4.13) (100 kDa U5 snRNP-specific protein) (DEAD box protein 23) (PRP28 homolog) (U5-100kD)	Q9BUQ8
Q9UKR5	Probable ergosterol biosynthetic protein 28	Q9UKR5

A2RTX5	Probable threonine--tRNA ligase 2, cytoplasmic (EC 6.1.1.3) (Threonyl-tRNA synthetase) (ThrRS) (Threonyl-tRNA synthetase-like protein 2)	A2RTX5;A2RTX5-2;E7ERI3;G3XAN9;P26639;P26639-2
B4DR87	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1#	B4DR87;Q02809
C9JU11	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 3	C9JU11;H7C2A8;O60568
K7EJ44	Profilin 1, isoform CRA_b (Profilin-1)	K7EJ44;P07737
Q8WUM4	Programmed cell death 6-interacting protein (PDCD6-interacting protein) (ALG-2-interacting protein 1) (ALG-2-interacting protein X) (Hp95)	Q8WUM4;Q8WUM4-2;C9IZF9;F8WBR8;F8WEQ8
K7ESJ4	Programmed cell death protein 5	K7ESJ4;O14737;Q3HM38
C9JW96	Prohibitin	C9JW96;C9JZ20;E7ESE2;E9PCW0;P35232
F5GWA7	Prohibitin-2	F5GWA7;F5GY37;J3KPX7;Q99623
F8VR77	Proliferation-associated protein 2G4 (Cell cycle protein p38-2G4 homolog) (hG4-1) (ErbB3-binding protein 1)	F8VR77;Q9UQ80
P48147	Prolyl endopeptidase (PE) (EC 3.4.21.26) (Post-proline cleaving enzyme)	P48147
Q9UHG2	ProSAAS (Proprotein convertase subtilisin/kexin type 1 inhibitor) (Proprotein convertase 1 inhibitor) (pro-SAAS) [Cleaved into: KEP; Big SAAS (b-SAAS); Little SAAS (l-SAAS) (N-proSAAS); Big PEN-LEN (b-PEN-LEN) (SAAS CT(1-49)); PEN; Little LEN (l-LEN); Big LEN (b-LEN) (SAAS CT(25-40))]	Q9UHG2
O15354	Prosaposin receptor GPR37 (Endothelin B receptor-like protein 1) (ETBR-LP-1) (G-protein coupled receptor 37) (Parkin-associated endothelin receptor-like receptor) (PAELR)	O15354
Q16186	Proteasomal ubiquitin receptor ADRM1 (110 kDa cell membrane glycoprotein) (Gp110) (Adhesion-regulating molecule 1) (ARM-1) (Proteasome regulatory particle non-ATPase 13) (hRpn13) (Rpn13 homolog)	Q16186
B4DEV8	Proteasome subunit alpha type (EC 3.4.25.1)	B4DEV8;F5GX11;P25786;P25786-2
F5GX11	Proteasome subunit alpha type-1	F5GX11;P25786;P25786-2
G3V4X5	Proteasome subunit alpha type-3 (EC 3.4.25.1) (Macropain subunit C8) (Multicatalytic endopeptidase complex subunit C8) (Proteasome component C8)	G3V4X5;P25788;P25788-2
H0YN18	Proteasome subunit alpha type-4	H0YN18;P25789;P25789-2
P28066	Proteasome subunit alpha type-5 (EC 3.4.25.1) (Macropain zeta chain) (Multicatalytic endopeptidase complex zeta chain) (Proteasome zeta chain)	P28066;P28066-2
H0Y586	Proteasome subunit alpha type-7	H0Y586;O14818;O14818-2;Q8TAA3;Q8TAA3-2;Q8TAA3-5
P20618	Proteasome subunit beta type-1 (EC 3.4.25.1) (Macropain subunit C5) (Multicatalytic endopeptidase complex subunit C5) (Proteasome component C5) (Proteasome gamma chain)	P20618

P49721	Proteasome subunit beta type-2 (EC 3.4.25.1) (Macropain subunit C7-I) (Multicatalytic endopeptidase complex subunit C7-I) (Proteasome component C7-I)	P49721
J3KRR2	Proteasome subunit beta type-3	J3KRR2;J3KSM3;J3QKR3;P49720
P28070	Proteasome subunit beta type-4 (EC 3.4.25.1) (26 kDa prosomal protein) (HsBPROS26) (PROS-26) (Macropain beta chain) (Multicatalytic endopeptidase complex beta chain) (Proteasome beta chain) (Proteasome chain 3) (HsN3)	P28070
P28074	Proteasome subunit beta type-5 (EC 3.4.25.1) (Macropain epsilon chain) (Multicatalytic endopeptidase complex epsilon chain) (Proteasome chain 6) (Proteasome epsilon chain) (Proteasome subunit MB1) (Proteasome subunit X)	P28074;P28074-3
E9PIX6	Protein arginine N-methyltransferase 1	E9PIX6;E9PKG1;E9PQ98;H7C2I1;Q99873;Q99873-2;Q99873-3;Q99873-4
O14744	Protein arginine N-methyltransferase 5 (EC 2.1.1.-) (72 kDa ICln-binding protein) (Histone-arginine N-methyltransferase PRMT5) (EC 2.1.1.125) (Jak-binding protein 1) (Shk1 kinase-binding protein 1 homolog) (SKB1 homolog) (SKB1Hs) [Cleaved into: Protein arginine N-methyltransferase 5, N-terminally processed]	O14744;O14744-2
F8WCF6	Protein ARPC4-TTLL3	F8WCF6;F8WDD7;P59998;P59998-2;P59998-3
C9JNV2	Protein BUD31 homolog	C9JNV2;P41223;P41223-2
Q9BT09	Protein canopy homolog 3 (CTG repeat protein 4a) (Expanded repeat-domain protein CAG/CTG 5) (Protein associated with TLR4) (Trinucleotide repeat-containing gene 5 protein)	Q9BT09
Q9UKY7	Protein CDV3 homolog	Q9UKY7;Q9UKY7-2
Q5TDH0	Protein DDI1 homolog 2	Q5TDH0;Q5TDH0-2;Q5TDH0-3
B4DFG0	Protein DEK (cD FLJ53031, highly similar to Protein DEK)	B4DFG0;D6R9L5;P35659
G5EA52	Protein disulfide isomerase family A, member 3, isoform CRA_b (Protein disulfide-isomerase A3)	G5EA52;P30101
I3L312	Protein disulfide-isomerase	I3L312;I3L3P5;P07237
P13667	Protein disulfide-isomerase A4 (EC 5.3.4.1) (Endoplasmic reticulum resident protein 70) (ER protein 70) (ERp70) (Endoplasmic reticulum resident protein 72) (ER protein 72) (ERp-72) (ERp72)	P13667
Q15084	Protein disulfide-isomerase A6 (EC 5.3.4.1) (Endoplasmic reticulum protein 5) (ER protein 5) (ERp5) (Protein disulfide isomerase P5) (Thioredoxin domain-containing protein 7)	Q15084-5;Q15084-3;Q15084-4;Q15084;Q15084-2
K7ELW0	Protein DJ-1	Q99497;K7ELW0
Q5VUD6	Protein FAM69B	Q5VUD6;Q5VUD6-2
Q13045	Protein flightless-1 homolog	Q13045;Q13045-2;Q13045-3
F8VVB6	Protein kinase C-binding protein NELL2	F8VVB6;Q99435;Q99435-2;Q99435-3;Q99435-4

F8VVB6	Protein kise C-binding protein NELL2	F8VVB6;Q99435;Q99435-2;Q99435-3;Q99435-4
B4E2N0	Protein LZIC#	B4E2N0;K7ES95;Q8WZA0
E9PL57	Protein NEDD8-MDP1	E9PL57;E9PS38;F8VSA6;H3BP08;H3BTT7;Q15011;Q15011-2;Q15011-3;Q15011-4;Q15843;S4R3E9
F6XY72	Protein NME1-NME2	F6XY72;O60361;P22392;P22392-2;Q32Q12
Q9BVG4	Protein PBDC1 (Polysaccharide biosynthesis domain-containing protein 1)	A6NDF3;P11532;E9PDN5;P11532-4;Q4G0X0;Q9BVG5
O15355	Protein phosphatase 1G (EC 3.1.3.16) (Protein phosphatase 1C) (Protein phosphatase 2C isoform gamma) (PP2C-gamma) (Protein phosphatase magnesium-dependent 1 gamma)	O15355
E7EVG2	Protein polybromo-1	E7EVG2;H0Y5B5;Q86U86;Q86U86-2;Q86U86-3;Q86U86-4;Q86U86-5;Q86U86-6;Q86U86-7;Q86U86-8;Q86U86-9
Q9P258	Protein RCC2 (RCC1-like protein TD-60) (Telophase disk protein of 60 kDa)	Q9P258
O15258	Protein RER1	O15258;Q5T091;Q5T092
H0Y3V9	Protein RPL36A-HNRNPH2	H0Y3V9;H0Y5B4;H7BY91;H7BZ11;J3KQN4;P83881
Q14690	Protein RRP5 homolog (NF-kappa-B-binding protein) (NFBP) (Programmed cell death protein 11)	Q14690
P60903	Protein S100-A10 (Calpactin I light chain) (Calpactin-1 light chain) (Cellular ligand of annexin II) (S100 calcium-binding protein A10) (p10 protein) (p11)	P60903
P26447	Protein S100-A4 (Calvasculin) (Metastasin) (Placental calcium-binding protein) (Protein Mts1) (S100 calcium-binding protein A4)	P26447
Q01105	Protein SET (HLA-DR-associated protein II) (Inhibitor of granzyme A-activated Dse) (IGAAD) (PHAPII) (Phosphatase 2A inhibitor I2PP2A) (I-2PP2A) (Template-activating factor I) (TAF-I)	Q01105;Q01105-2;Q01105-3;Q01105-4
P0DME0	Protein SETSIP (SET pseudogene protein 18) (SET similar protein) (Similar to SET translocation protein)	Q01105;Q01105-2;Q01105-3;Q01105-4;P0DME0
A6NIF9	Protein transport protein Sec61 subunit alpha isoform 2	A6NIF9;A6NK38;B4DR61;C9JJV4;C9JXC6;F2Z2C7;F8W776;H7C069;H7C1Q9;P61619;Q8TC24;Q9H9S3;Q9H9S3-2;Q9H9S3-3
B7Z972	Protein-L-isoaspartate O-methyltransferase (EC 2.1.1.77)	B7Z972;C9J0F2;H7BY58;P22061;P22061-2
H0Y6Z4	Protein-methionine sulfoxide oxidase MICAL1	H0Y6Z4;Q8TDZ2;Q8TDZ2-2;Q8TDZ2-4
H0YA52	Pterin-4-alpha-carbinolamine dehydratase 2	H0YA52;P61457;Q9H0N5
K7ENC1	Purine-rich element-binding protein gamma	Q00577;Q96QR8;Q9H598;K7ENC1;Q9UJV8;Q9UJV8-2
B7Z463	Puromycin-sensitive aminopeptidase#	B7Z463;E9PLK3;P55786
B2RPK0	Putative high mobility group protein B1-like 1 (High mobility group protein B1 pseudogene 1) (Putative high mobility group protein 1-like 1) (HMG-1L1)	B2RPK0;P09429;P23497;Q5T7C0;Q5T7C4;Q5T7C6
A6NI72	Putative neutrophil cytosol factor 1B (NCF-1B) (Putative SH3 and PX domain-containing protein 1B)	A6NI72;C9J155;P14598;P14598-2

A2A3N6	Putative PIP5K1A and PSMD4-like protein (PIP5K1A-PSMD4)	A2A3N6;A6PVX3;P55036;P55036-2;Q5VWC4
O43143	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15 (EC 3.6.4.13) (ATP-dependent RNA helicase #46) (DEAH box protein 15)	O43143
P98179	Putative RNA-binding protein 3 (RNA-binding motif protein 3) (RNPL)	P98179
A8MWD9	Putative small nuclear ribonucleoprotein G-like protein 15	A8MWD9;C9JVQ0;P62308
H3BQ34	Pyruvate kinase (EC 2.7.1.40)	H3BQ34;H3BTN5;P14618;P14618-2;P14618-3
P30613	Pyruvate kinase PKLR (EC 2.7.1.40) (Pyruvate kinase 1) (Pyruvate kinase isozymes L/R) (R-type/L-type pyruvate kinase) (Red cell/liver pyruvate kinase)	P30613;P30613-2
E9PNV3	Radixin	P35241;P35241-3;P35241-5;E9PNV3
C9JDM3	Ran-specific GTPase-activating protein	C9JIC6;C9JJ34;C9JXG8;P43487;C9JDM3;C9JGV6;P43487-2
E5RH42	Ras GTPase-activating protein-binding protein 1	E5RH42;E5RI46;E5RIF8;E5RIZ6;E5RJU8;Q13283;Q5HYE9
H0YLE8	Ras GTPase-activating-like protein IQGAP1	H0YLE8;P46940
B1AH77	Ras-related C3 botulinum toxin substrate 1 (Cell migration-inducing gene 5 protein) (Ras-like protein TC25) (p21-Rac1)	B1AH77;B1AH80;P15153;P63000;P63000-2;B1AH78
P61026	Ras-related protein Rab-10	P61026
Q6IQ22	Ras-related protein Rab-12	Q6IQ22
P51153	Ras-related protein Rab-13 (Cell growth-inhibiting gene 4 protein)	P51153;P61026
P61106	Ras-related protein Rab-14	P61106;X6RFL8
E9PKL7	Ras-related protein Rab-2A	E9PKL7;H0YD31;P61019;P61019-2
F5H157	Ras-related protein Rab-35	F5H157;Q15286
F8VSF8	Ras-related protein Rab-5C	F8VVK3;K7ERI8;K7ERQ8;P51148;P51148-2;F8VWU4;F8VSF8
C9IZZ0	Ras-related protein Rab-7a	C9IZZ0;C9J4S4;C9J4V0;C9J592;C9J7D1;C9J8S3;P51149
B4DEK7	Ras-related protein Rab-8A#	B4DEK7;B7Z8M7;E7END7;E7ETK2;E9PLD0;F5GY21;H0YL94;H0YLJ8;H0YMN7;H0YNE9;P51153;P59190;P59190-2;P61006;P61026;P62820;P62820-2;P62820-3;Q92928;Q92930;Q9H0U4;F5H157;Q15286;Q15286-2
H7C3P7	Ras-related protein Ral-A	H7C3P7;P11233
E7ESV4	Ras-related protein Rap-1b	E7ESV4;F5GWU8;F5GX62;F5GYB5;F5GYH7;F5H004;F5H077;F5H0B7;F5H491;F5H4H0;F5H500;F5H6R7;F5H7Y6;F8WBC0;P61224;P61224-2;P61224-3;P61224-4;P62834
A6NIZ1	Ras-related protein Rap-1b-like protein	A6NIZ1;E7ESV4;F5GWU8;F5GX62;F5GYB5;F5GYH7;F5H004;F5H0B7;F5H491;F5H4H0;F5H500;F5H6R7;F5H7Y6;P61224;P61224-2;P61224-3;P62834;F5H077
Q96PK6	R-binding protein 14 (Paraspeckle protein 2) (PSP2) (R-binding motif protein 14) (RRM-containing coactivator activator/modulator) (Syptotagmin-interacting protein) (SYT-interacting protein)	Q96PK6

D6R9K7	R-binding protein 4	D6R9K7;E9PB51;E9PLB0;E9PM61;J3QR R5;Q9BQ04;Q9BWF3;Q9BWF3-2;Q9BWF 3-3;Q9BWF3-4;U3KQD5
H3BPE7	R-binding protein FUS	H3BPE7;P35637;P35637-2;K7EPT6;Q928 04;Q92804-2
P23471	Receptor-type tyrosine-protein phosphatase zeta (R-PTP-zeta) (EC 3.1.3.48) (Protein-tyrosine phosphatase receptor type Z polypeptide 1) (Protein-tyrosine phosphatase receptor type Z polypeptide 2) (R-PTP-zeta-2)	P23471-3;P23471;P23471-2
J3KQ66	Reelin	J3KQ66;P78509;P78509-2;P78509-3
A2A2M0	Regulation of nuclear pre-mRNA domain-containing protein 1B	A2A2M0;Q9NQG5
Q92900	Regulator of nonsense transcripts 1 (EC 3.6.4.-) (ATP-dependent helicase RENT1) (Nonsense mR reducing factor 1) (NORF1) (Up-frameshift suppressor 1 homolog) (hUpf1)	Q92900;Q92900-2
Q86UN3	Reticulon-4 receptor-like 2 (Nogo receptor-like 3) (Nogo-66 receptor homolog 1) (Nogo-66 receptor-related protein 2) (NgR2)	Q86UN3
B7Z6Z4	Retinal cone rhodopsin-sensitive cGMP 3',5'-cyclic phosphodiesterase subunit gamma (cDNA FLJ56329, highly similar to Myosin light polypeptide 6)	B7Z6Z4;F8VPF3;F8W1I5;F8W1R7;G3V1V 0;G8JLA2;J3KND3;P14649;P60660;P6066 0-2
I3L2N6	Retinoid-inducible serine carboxypeptidase	I3L2N6;I3L4Z3;Q9HB40;Q9HB40-2
J3KNF6	RGM domain family member B	J3KNF6;Q6NW40
J3KTF8	Rho GDP-dissociation inhibitor 1	J3QQX2;P52565;J3KTF8
F5H2R5	Rho GDP-dissociation inhibitor 2	F5H2R5;F5H6Q0;H0YGX7;P52566;F5H3P 3
E9PNR6	Rho GTPase-activating protein 1	E9PNR6;H0YE29;Q07960
Q5TBB1	Ribonuclease H2 subunit B (RNase H2 subunit B) (Aicardi-Goutieres syndrome 2 protein) (AGS2) (Deleted in lymphocytic leukemia 8) (Ribonuclease H1 subunit B)	Q5TBB1-2;Q5TBB1
E9PAU2	Ribonucleoprotein PTB-binding 1	E9PAU2;Q8IY67-2
E7ENU7	Ribosomal protein L15	E7ENU7;E7EQV9;P61313
B1AXG1	Ribosomal protein S6 kinase alpha-3	B7Z3B5;D6R910;F2Z2J1;J3KRK0;J3QLK5 ;Q15349;Q15349-2;Q15349-3;Q5TI62;Q86 UE8;Q86UE8-2;Q86UE8-3;Q9UKI8;Q9UKI 8-2;Q9UKI8-3;Q9UKI8-4;Q9UKI8-5;B1AXG 1;B4DG22;B7ZB17;B7ZL90;E7ERL6;E7E WQ5;E9PGT3;E9PRI4;F5GYC4;F8WAQ9; J3QT34;O15021;O15021-1;O15021-2;O15 021-3;O60307;P51812;Q15418;Q15418-2; Q15418-3;Q6P0Q8;Q6P0Q8-2;Q96GX5;Q 96GX5-2;Q96GX5-3;Q9UK32;Q9Y2H9;V9 GXZ1
Q9Y3A5	Ribosome maturation protein SBDS (Shwachman-Bodian-Diamond syndrome protein)	Q9Y3A5
Q5VXN0	Ribosome production factor 2 homolog	Q5VXN0;Q9H7B2
F8W7S5	Ribosome-binding protein 1	F8W7S5;Q9P2E9;Q9P2E9-2;Q9P2E9-3
Q96PK6	RNA-binding protein 14 (Paraspeckle protein 2) (PSP2) (RNA-binding motif protein 14) (RRM-containing coactivator activator/modulator) (Synaptotagmin-interacting	Q96PK6;Q96PK6-2

	protein) (SYT-interacting protein)	
H3BPE7	RNA-binding protein FUS	H3BPE7;P35637;P35637-2
Q9NRX1	RNA-binding protein PNO1	Q9NRX1
Q5QPL9	RNA-binding protein Raly	Q5QPL9;Q9UKM9;Q9UKM9-2;Q5QPM0
M0QXL5	rR 2'-O-methyltransferase fibrillarin	M0QXL5;M0R0P1;M0R1H0;M0R299;M0R2B0;M0R2Q4;M0R2U2;P22087
M0QXL5	rRNA 2'-O-methyltransferase fibrillarin	M0QXL5;M0R0P1;M0R1H0;M0R299;M0R2B0;M0R2Q4;M0R2U2;P22087
A6NHQ2	rRNA/tRNA 2'-O-methyltransferase fibrillarin-like protein 1 (EC 2.1.1.-) (Protein-glutamine methyltransferase)	M0QXL5;M0R0P1;M0R299;M0R2Q4;P22087;A6NHQ2;R4GMW7
Q5JTH9	RRP12-like protein	Q5JTH9;Q5JTH9-2;Q5JTH9-3
E7ETR0	RuvB-like 1	E7ETR0;H7C4G5;H7C4I3;Q9Y265;Q9Y265-2
H7BXE3	SAFB-like transcription modulator	H7BXE3;Q9NWH9
B1AVU8	Saposin-D	B1AVU8;C9JIZ6;P07602;P07602-2;P07602-3
H7C5W9	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	H7C5W9;P16615;P16615-2;P16615-3;P16615-4;P16615-5;Q93084;Q93084-2;Q93084-3;Q93084-4;Q93084-5;Q93084-6;Q93084-7
E9PAV3	scent polypeptide-associated complex subunit alpha, muscle-specific form (Alpha-C, muscle-specific form) (skC)	E9PAV3;F8VNW4;F8VZJ2;F8W0W4;F8W1N5;H0YHX9;Q13765;Q13765-2
P05060	Secretogranin-1 (Chromogranin-B) (CgB) (Secretogranin I) (SgI) [Cleaved into: GAWK peptide; CCB peptide]	P05060
P13521	Secretogranin-2 (Chromogranin-C) (Secretogranin II) (SgII) [Cleaved into: Secretoneurin (SN)]	P13521
Q8WXD2	Secretogranin-3 (Secretogranin III) (SgIII)	Q8WXD2
C9JQI2	Secretoneurin	P13521;C9JQI2
B0QYH4	Seizure 6-like protein	B0QYH4;B0QYH5;Q9BYH1;Q9BYH1-2;Q9BYH1-3;Q9BYH1-4;Q9BYH1-5;Q9BYH1-6;Q9BYH1-7
F5GYX3	Semaphorin-7A	F5GYX3;O75326;O75326-2
B5MCX3	Septin-2	B5MCX3;H7C2Y0;Q15019;Q15019-2
E7EPK1	Septin-7	E7EPK1;E7ES33;G3V1Q4;Q16181;Q16181-2;Q5JXL7
K7EIE4	Septin-9	K7EIE4;K7EK18;K7EL40;K7ELJ9;K7EQD7;K7ER52;Q9UHD8;Q9UHD8-2;Q9UHD8-3;Q9UHD8-4;Q9UHD8-5;Q9UHD8-7;Q9UHD8-8;Q9UHD8-9
G3V241	Serine hydroxymethyltransferase, mitochondrial	P34897;P34897-2;P34897-3;G3V241;G3V2E4;G3V2W0;G3V3Y8;G3V4T0;G3V4W5;G3V4X0;G3V540;G3V5L0
Q92743	Serine protease HTRA1 (EC 3.4.21.-) (High-temperature requirement A serine peptidase 1) (L56) (Serine protease 11)	Q92743
B4E241	Serine/arginine-rich splicing factor 3#	B4E241;P84103
J3KSW7	Serine/arginine-rich-splicing factor 1	J3KSW7;J3KTL2;J3QQV5;Q07955;Q07955-2;Q07955-3
C9JAB2	Serine/arginine-rich-splicing factor 7	C9JAB2;Q16629;Q16629-2;Q16629-3;Q16629-4
O94804	Serine/threonine-protein kinase 10 (EC 2.7.11.1) (Lymphocyte-oriented kinase)	O94804;Q9H2G2;Q9H2G2-2

Q13177	Serine/threonine-protein kinase PAK 2 (EC 2.7.11.1) (Gamma-PAK) (PAK65) (S6/H4 kinase) (p21-activated kinase 2) (PAK-2) (p58) [Cleaved into: PAK-2p27 (p27); PAK-2p34 (p34) (C-t-PAK2)]	Q13177
B1AKS5	Serine/threonine-protein kinase PAK 3	Q13177;B1AKS5;O75914;O75914-2;O75914-3;O75914-4
E9PMD7	Serine/threonine-protein phosphatase (EC 3.1.3.16)	E9PMD7;F8VYE8;F8W0W8;P36873;P36873-2;P62136;P62136-2;P62136-3;P62140
E5RFR9	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B alpha isoform	E5RFR9;P63151;P63151-2;Q9Y2T4;Q9Y2T4-2;Q9Y2T4-3;Q9Y2T4-4
B3KQV6	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform (cD FLJ33169 fis, clone ADRGL2000384, highly similar to Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform)	B3KQV6;C9J9C1;F5H3X9;J3KR29;P30153;P30154;P30154-2;P30154-3;P30154-4
A6PVN5	Serine/threonine-protein phosphatase 2A activator	A6PVN5;A6PVN9;B4DZF8;H0Y562;H0Y6E5;Q15257;Q15257-2;Q15257-3;Q15257-4
Q08209	Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform (EC 3.1.3.16) (CAM-PRP catalytic subunit) (Calmodulin-dependent calcineurin A subunit alpha isoform)	Q08209-2;Q08209-3
B4DNJ6	Serine-threonine kinase receptor-associated protein (cDNA FLJ51909, highly similar to Serine-threonine kinase receptor-associated protein)	B4DNJ6;Q9Y3F4
P49591	Serine--tR ligase, cytoplasmic (EC 6.1.1.11) (Seryl-tR synthetase) (SerRS) (Seryl-tR(Ser/Sec) synthetase)	P49591;Q5T5C7
J3KN47	Serotransferrin	C9JVG0;J3KN47;P02786
C9JTJ8	Serpin B8	C9JTJ8;C9JVA8;H7BXX7;P35237;P50452;P50452-2
Q9BXP5	Serratia RNA effector molecule homolog (Arsenite-resistance protein 2)	H7C3A1;Q9BXP5;Q9BXP5-2;Q9BXP5-3;Q9BXP5-4;Q9BXP5-4
B7WNR0	Serum albumin	B7WNR0;C9JKR2;H7C013;P02768;P02768-2
C9JZ99	Serum paraoxonase/lactonase 3	C9JZ99;F8WD41;Q15166;F5H4W9;P27169
P10768	S-formylglutathione hydrolase (FGH) (EC 3.1.2.12) (Esterase D) (Methylumbelliferyl-acetate deacetylase) (EC 3.1.1.56)	P10768
O75368	SH3 domain-binding glutamic acid-rich-like protein	O75368
H0YKT4	Signal peptidase complex catalytic subunit SEC11A	P67812-4;P67812-3;H0YKT4;H0YNG3;P67812;P67812-2
E9PI68	Signal peptidase complex subunit 2	E9PI68;E9PL01;H0YE04;Q15005
G3V346	Signal recognition particle 54 kDa protein	G3V3L9;G3V480;P61011;G3V346
H0Y9L6	Sister chromatid cohesion protein PDS5 homolog A	H0Y9L6;Q29RF7
Q5T0V3	Slit homolog 1 protein	Q5T0V3
K7EJB5	Small nuclear ribonucleoprotein Sm D2	P62316;P62316-2;K7EJB5
B3KVR1	Small nuclear ribonucleoprotein-associated protein N#	B3KVR1;J3KRY3;J3QLE5;P14678;P14678-2;P14678-3;P63162;S4R3P3

B4DUC8	S-methyl-5'-thioadenosine phosphorylase (EC 2.4.2.28) (5'-methylthioadenosine phosphorylase)	B4DUC8;F2Z2F3;J3QSB7;Q13126;Q13126-2;Q13126-3;Q13126-4;Q13126-5;Q13126-6;Q13126-7
B8ZZ67	SMT3 suppressor of mif two 3 homolog 1 (Yeast), isoform CRA_b (Small ubiquitin-related modifier 1)	B8ZZ67;B8ZZN6;P63165;P63165-2
G3V3A4	SNW domain-containing protein 1	G3V3A4;G3V4X8;Q13573
P05023	Sodium/potassium-transporting ATPase subunit alpha-1 (Na(+)/K(+) ATPase alpha-1 subunit) (EC 3.6.3.9) (Sodium pump subunit alpha-1)	P05023;P05023-2;P05023-3;P05023-4
B1AKY9	Sodium/potassium-transporting ATPase subunit alpha-2	B1AKY9;M0R116;P05023;P05023-2;P05023-3;P05023-4;P13637;P13637-2;P13637-3;P20648;P50993
M0R116	Sodium/potassium-transporting ATPase subunit alpha-3	M0R116;P05023;P05023-3;P05023-4;P13637;P13637-2;P13637-3;Q5TC05
F8VX04	Sodium-coupled neutral amino acid transporter 1	F8VX04;Q9H2H9
P61278	Somatostatin (Growth hormone release-inhibiting factor) [Cleaved into: Somatostatin-28; Somatostatin-14]	P61278
C9J0K6	Sorcin	P30626-3;C9J0K6;P30626;P30626-2
B4DJS7	Sorting nexin 6, isoform CRA_e (cDNA FLJ58001, highly similar to Sorting nexin-6)	B4DJS7;Q9UNH7;Q9UNH7-2
Q9UMY4	Sorting nexin-12	Q9UMY4;Q9UMY4-2
B4DEK4	Sorting nexin-2	B4DEK4;O60749;E9PS65;H7C5W5;P41219;P41219-2
Q96L92	Sorting nexin-27	Q96L92;Q96L92-3
O60493	Sorting nexin-3 (Protein SDP3)	O60493;O60493-3;O60493-4
G3V2U1	Sorting nexin-6	G3V5X9;Q9UNH7;G3V2U1;G3V4Z5;H0YJF8
E5RK62	SPARC	E5RK62;F5GY03;P09486
C9JJR8	SPARC-like protein 1	C9JJR8;D6RA29;F5H331;F5H4Y3;Q14515;E9PC64
Q9H4F8	SPARC-related modular calcium-binding protein 1 (Secreted modular calcium-binding protein 1) (SMOC-1)	Q9H4F8;Q9H4F8-2
E5RJR5	S-phase kinase-associated protein 1	E5RJR5;P63208
O75533	Splicing factor 3B subunit 1 (Pre-mRNA-splicing factor SF3b 155 kDa subunit) (SF3b155) (Spliceosome-associated protein 155) (SAP 155)	H7C341;O75534
Q15393	Splicing factor 3B subunit 3 (Pre-mR-splicing factor SF3b 130 kDa subunit) (SF3b130) (STAF130) (Spliceosome-associated protein 130) (SAP 130)	Q15393;Q15393-2
Q15427	Splicing factor 3B subunit 4 (Pre-mRNA-splicing factor SF3b 49 kDa subunit) (SF3b50) (Spliceosome-associated protein 49) (SAP 49)	Q15427
H0Y6J6	Splicing factor 45	H0Y6J6;Q5W010;Q5W011;Q5W012;Q96I25
K7ENG2	Splicing factor U2AF 65 kDa subunit	K7ENG2;P26368;P26368-2
P23246	Splicing factor, proline- and glutamine-rich (100 kDa DNA-pairing protein) (hPOMp100) (DNA-binding p52/p100 complex, 100 kDa subunit) (Polypyrimidine tract-binding protein-associated-splicing factor) (PSF) (PTB-associated-splicing factor)	P23246;P23246-2

Q9HCB6	Spondin-1 (F-spondin) (Vascular smooth muscle cell growth-promoting factor)	Q9HCB6
Q7KZF4	Staphylococcal nuclease domain-containing protein 1 (100 kDa coactivator) (EBNA2 coactivator p100) (Tudor domain-containing protein 11) (p100 co-activator)	H7C597;Q7KZF3
P16949	Stathmin (Leukemia-associated phosphoprotein p18) (Metablastin) (Oncoprotein 18) (Op18) (Phosphoprotein p19) (pp19) (Prosolin) (Protein Pr22) (pp17)	P16949;P16949-2;A2A2D1
P38646	Stress-70 protein, mitochondrial (75 kDa glucose-regulated protein) (GRP-75) (Heat shock 70 kDa protein 9) (Mortalin) (MOT) (Peptide-binding protein 74) (PBP74)	P38646
F5GXD8	Stress-induced-phosphoprotein 1 (ST11) (Hsc70/Hsp90-organizing protein) (Hop) (Renal carcinoma antigen NY-REN-11) (Transformation-sensitive protein IEF SSP 3521)	F5GXD8;P31948-3;F5H783;P31948-2;P31948
Q14683	Structural maintenance of chromosomes protein 1A (SMC protein 1A) (SMC-1-alpha) (SMC-1A) (Sb1.8)	Q14683
D6RFM5	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	D6RFM5;P31040-2;P31040;P31040-3
H7C233	Succinyl-CoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial	H7C233;P53597
P55809	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial (EC 2.8.3.5) (3-oxoacid CoA-transferase 1) (Somatic-type succinyl-CoA:3-oxoacid CoA-transferase) (SCOT-s)	P55809
O75683	Surfeit locus protein 6	O75683
C9K0U0	SUZ domain-containing protein 1	C9K0U0;F8WEE8;Q7Z422;Q7Z422-2;Q7Z422-3;Q7Z422-4
F8VXC8	SWI/SNF complex subunit SMARCC2	F8VXC8;Q8TAQ2;Q8TAQ2-2;Q8TAQ2-3;Q92922
O60264	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A member 5 (SWI/SNF-related matrix-associated actin-dependent regulator of chromatin A5) (EC 3.6.4.-) (Sucrose nonfermenting protein 2 homolog) (hSNF2H)	O60264;P28370;P28370-2
O15498	Synaptobrevin homolog YKT6 (EC 2.3.1.-)	O15498
Q9H7C4	Syncoilin (Syncoilin intermediate filament 1) (Syncoilin-1)	Q9H7C4
B1AJQ6	Syntaxin-12	B1AJQ6;Q86Y82
O15400	Syntaxin-7	O15400;O15400-2
I3L305	Syntaxin-8	I3L305;Q9UNK0
P61764	Syntaxin-binding protein 1 (MUNC18-1) (N-Sec1) (Protein unc-18 homolog 1) (Unc18-1) (Protein unc-18 homolog A) (Unc-18A) (p67)	P61764;P61764-2
Q5TCU6	Talin-1	Q9Y490;Q5TCU6
H0YMT1	Talin-2	H0YMT1;Q5TCU6;Q9Y490;Q9Y4G6
E7EQR6	T-complex protein 1 subunit alpha	E7EQR6;F5H282;P17987
F5GWF6	T-complex protein 1 subunit beta	F5GWF6;F8VQ14;P78371;P78371-2

B7ZAR1	T-complex protein 1 subunit epsilon (cDNA, FLJ79275, highly similar to T-complex protein 1 subunit epsilon)	P48643-2;B7ZAR1;E7ENZ3;E9PCA1;P48643
B4DUR8	T-complex protein 1 subunit gamma (cD FLJ57603, highly similar to T-complex protein 1 subunit gamma) (cD, FLJ78822, highly similar to T-complex protein 1 subunit gamma) (cD, FLJ79286, highly similar to T-complex protein 1 subunit gamma)	E9PM09;E9PRC8;P49368;P49368-2;Q5SZW8;Q5SZX6;Q5SZX8
P50990	T-complex protein 1 subunit theta (TCP-1-theta) (CCT-theta) (Renal carcinoma antigen NY-REN-15)	P50990-2;P50990-3;P50990
P10599	Thioredoxin (Trx) (ATL-derived factor) (ADF) (Surface-associated sulphhydryl protein) (SASP)	P10599;P10599-2
P30048	Thioredoxin-dependent peroxide reductase, mitochondrial (EC 1.11.1.15) (Antioxidant protein 1) (AOP-1) (HBC189) (Peroxiredoxin III) (Prx-III) (Peroxiredoxin-3) (Protein MER5 homolog)	P30048-2;P30048
K7EKG2	Thioredoxin-like protein 1	K7EKG2;K7EPB7;O43396
E9PB61	THO complex subunit 4	E9PB61;Q86V81
D6R9F8	Threonine--tR ligase, cytoplasmic	P26639;P26639-2;D6R9F8;D6RBR8;D6RCA5;D6RDJ6
C9JV37	Thrombin light chain	C9JV37;E9PIT3;P00734
E9PIM6	Thy-1 membrane glycoprotein	E9PNQ8;P04216;E9PIM6
B8ZZA1	Thymosin alpha-1	B8ZZA1;B8ZZQ6;B8ZZW7;H7C2N1;P06454;P06454-2
O75663	TIP41-like protein (Putative MAPK-activating protein PM10) (Type 2A-interacting protein) (TIP)	O75663;O75663-2
Q08J23	tR (cytosine(34)-C(5))-methyltransferase (EC 2.1.1.203) (Myc-induced SUN domain-containing protein) (Misu) (NOL1/NOP2/Sun domain family member 2) (Substrate of AIM1/Aurora kinase B) (tR (cytosine-5-)-methyltransferase) (tR methyltransferase 4 homolog) (hTrm4)	Q08J23;Q08J23-2
C9J338	TRAF2 and NCK-interacting protein kinase	C9J338;E7EN19;E7ENQ1;E7ESS2;F5H5M9;F5H865;G3XAA2;G5E948;H7C360;I3L2I2;O95819;O95819-2;O95819-3;O95819-4;O95819-5;Q8N4C8;Q8N4C8-2;Q8N4C8-3;Q8N4C8-4;Q8N4C8-5;Q9UKE5;Q9UKE5-2;Q9UKE5-3;Q9UKE5-4;Q9UKE5-5;Q9UKE5-6;Q9UKE5-7;Q9UKE5-8
P37837	Transaldolase (EC 2.2.1.2)	P37837
B5MBX2	Transcobalamin-2	B5MBX2;P20062;P20062-2;C9J6W9
B8ZZU8	Transcription elongation factor B (SIII), polypeptide 2 (18kDa, elongin B), isoform CRA_b (Transcription elongation factor B polypeptide 2)	B8ZZU8;I3L0M9;Q15370;Q15370-2
E5RHG8	Transcription elongation factor B polypeptide 1	E5RHG8;Q15369;Q15369-2
O15391	Transcription factor YY2 (Yin and yang 2) (YY-2) (Zinc finger protein 631)	O15391;P25490
F2Z2U4	Transformation/transcription domain-associated protein	Q9BPX3;O75083;O75083-3;Q8WZ42;F2Z2U4;H0Y4W2;Q8WZ42-10;Q8WZ42-11;Q8WZ42-12;Q8WZ42-13;Q8WZ42-2;Q8WZ42-3;Q8WZ42-4;Q8WZ42-5;Q8WZ42-7;Q8WZ42-8;Q8WZ42-9;Q9Y4A5;Q9Y4A5-2
E7EMZ9	Transforming acidic coiled-coil-containing protein	O95359;E7EMZ9;E9PBC6;O95359-3

	2	
C9JNR4	Transforming protein RhoA	C9JNR4;C9JX21;E9PN11;E9PQH6;P08134;P61586;Q5JR05;Q5JR07;Q5JR08
P55072	Transitional endoplasmic reticulum ATPase (TER ATPase) (EC 3.6.4.6) (15S Mg(2+)-ATPase p97 subunit) (Valosin-containing protein) (VCP)	P55072
B4E022	Transketolase (cDNA FLJ56274, highly similar to Transketolase (EC 2.2.1.1))	B4E022;P29401;P29401-2
Q92616	Translational activator GCN1 (HsGCN1) (GCN1-like protein 1)	Q92616
E9PGT1	Translin	E9PGT1;Q15631
Q5TB53	Transmembrane 9 superfamily member 3	Q9HD45;Q5TB53
Q92544	Transmembrane 9 superfamily member 4	Q92544
G3V2K7	Transmembrane emp24 domain-containing protein 10 (21 kDa transmembrane-trafficking protein) (S31III125) (S31I125) (Tmp-21-I) (Transmembrane protein Tmp21) (p23) (p24 family protein delta-1) (p24delta1) (p24delta)	G3V2K7;P49755
E7EQ72	Transmembrane emp24 domain-containing protein 2	E7EQ72;Q15363
Q7Z7H5	Transmembrane emp24 domain-containing protein 4 (Endoplasmic reticulum stress-response protein 25) (ERS25) (GMP25iso) (Putative NF-kappa-B-activating protein 156) (p24 family protein alpha-3) (p24alpha3)	Q7Z7H5;Q7Z7H5-2;Q7Z7H5-3;F8W7F7
P40939	Trifunctional enzyme subunit alpha, mitochondrial (78 kDa gastrin-binding protein) (TP-alpha) [Includes: Long-chain enoyl-CoA hydratase (EC 4.2.1.17); Long chain 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.211)]	H0YFD6;P40938
P29144	Tripeptidyl-peptidase 2 (TPP-2) (EC 3.4.14.10) (Tripeptidyl aminopeptidase) (Tripeptidyl-peptidase II) (TPP-II)	P29144;Q5VZU9
B7Z596	Tropomyosin alpha-1 chain (cDNA FLJ55130, highly similar to Rattus norvegicus tropomyosin 1, alpha (Tpm1), transcript variant 8, mRNA)	B7Z596;F5H7S3;H0YK20;H0YK48;H0YKX5;H0YL42;H0YL52;H0YNC7;H7BYY1;J3KN67;K7EMU5;K7ENT6;K7EP68;K7EPV9;K7ERG3;P06753;P06753-2;P06753-3;P06753-4;P06753-5;P07951;P07951-2;P07951-3;P09493;P09493-10;P09493-2;P09493-3;P09493-4;P09493-5;P09493-6;P09493-7;P09493-8;P09493-9;P67936;P67936-2;Q5TCU3;Q5TCU8;P06753-6;Q5VU59;Q5VU61;P06753-7;Q6ZN40;U3KQK2
J3KN67	Tropomyosin alpha-3 chain	J3KN67;P06753-2;P06753-3;P06753-6;Q5VU59;Q5VU61
K7EPB9	Tropomyosin alpha-4 chain	K7EPB9;P67936;P67936-2
F5H5D3	Tubulin alpha-1C chain	F5H5D3;F8VQQ4;F8VRK0;F8VRZ4;F8VS66;F8VWV9;F8VX09;P68363;Q71U36;Q71U36-2;Q9BQE3;F8VVB9;P68363-2
C9JDS9	Tubulin alpha-4A chain	P68366-2;C9JDS9;C9JEV8;C9JJQ8;C9JQ00;F5H5D3;F8VQQ4;P68363;P68366;Q13748;Q13748-2;Q71U36;Q71U36-2;Q9BQE3
P07437	Tubulin beta chain (Tubulin beta-5 chain)	P07437;P68371;Q13885;Q5JP53;Q5ST81;Q9BVA1

Q13885	Tubulin beta-2A chain (Tubulin beta class IIa)	Q13885
P68371	Tubulin beta-4B chain (Tubulin beta-2 chain) (Tubulin beta-2C chain)	P68371
A6PVU8	Tuftelin	H0Y5R1;Q13029;Q13029-2;Q13029-3;Q5 THJ1;Q8WYA1;Q8WYA1-2;Q8WYA1-3;Q8 WYA1-4;Q8WYA1-5;Q8WYA1-6;Q8WYA1- 7;Q8WYA1-8;Q8WYA1-9;A6PVU8;F5H607 ;Q9NNX1;Q9NNX1-2;Q9NNX1-3
E5RFR7	Tumor protein D52	E5RFR7;F5H0B0;H0YC44;P55327;P5532 7-2;P55327-3;P55327-4;P55327-5;P55327 -6;P55327-7;P55327-8
F5H442	Tumor susceptibility gene 101 protein	F5H442;Q99816
Q86UY0	TXNDC5 protein (Thioredoxin domain-containing protein 5)	Q86UY0;Q8NBS9;Q8NBS9-2
Q06187	Tyrosine-protein kinase BTK (EC 2.7.10.2) (Agammaglobulinemia tyrosine kinase) (ATK) (B-cell progenitor kinase) (BPK) (Bruton tyrosine kinase)	Q06187;Q06187-2;Q5JY90
P78324	Tyrosine-protein phosphatase non-receptor type substrate 1 (SHP substrate 1) (SHPS-1) (Brain Ig-like molecule with tyrosine-based activation motifs) (Bit) (CD172 antigen-like family member A) (Inhibitory receptor SHPS-1) (Macrophage fusion receptor) (MyD-1 antigen) (Signal-regulatory protein alpha-1) (Sirp-alpha-1) (Signal-regulatory protein alpha-2) (Sirp-alpha-2) (Signal-regulatory protein alpha-3) (Sirp-alpha-3) (p84) (CD antigen CD172a)	P78324;P78324-2;P78324-4;Q5TFQ8
P54577	Tyrosine--tRNA ligase, cytoplasmic (EC 6.1.1.1) (Tyrosyl-tRNA synthetase) (TyrRS) [Cleaved into: Tyrosine--tRNA ligase, cytoplasmic, N-terminally processed]	P54577
P08621	U1 small nuclear ribonucleoprotein 70 kDa (U1 snRNP 70 kDa) (U1-70K) (snRNP70)	P08621;P08621-2;P08621-4
B4E0P5	U5 small nuclear ribonucleoprotein 200 kDa helicase (cDNA FLJ56901, highly similar to U5 small nuclear ribonucleoprotein 200 kDa helicase (EC 3.6.1.-))	B4E0P5;O75643
B4DQJ1	U5 small nuclear ribonucleoprotein 40 kDa protein#	B4DQJ1;Q96DI7;Q9NSS8
H0YDS0	Ubiquitin-1	H0YDS0;Q9NRR5;Q9UMX0;Q9UMX0-2
B4DV12	Ubiquitin (cDNA FLJ51326, highly similar to Homo sapiens ubiquitin B (UBB), mRNA)	B4DV12;F5GXX7;F5GYU3;F5GZ39;F5H04 1;F5H265;F5H2Z3;F5H388;J3QKN0;J3QL P7;J3QRK5;J3QS39;J3QSA3;J3QTR3;K7 EMA8;M0R1M6;M0R1V7;M0R2S1;P0CG4 7;P0CG48;P62979;P62987;Q96C32;F5H6 Q2;F5H747
P45974	Ubiquitin carboxyl-terminal hydrolase 5 (EC 3.4.19.12) (Deubiquitinating enzyme 5) (Isopeptidase T) (Ubiquitin thioesterase 5) (Ubiquitin-specific-processing protease 5)	P45974;P45974-2
P45974	Ubiquitin carboxyl-terminal hydrolase 5 (EC 3.4.19.12) (Deubiquitinating enzyme 5) (Isopeptidase T) (Ubiquitin thioesterase 5) (Ubiquitin-specific-processing protease 5)	P45974;P45974-2
F5GYJ8	Ubiquitin thioesterase OTUB1	F5GYJ8;F5GYN4;F5H6Q1;J3KR44;Q96F W1

F8W726	Ubiquitin-associated protein 2-like	F8W726;Q14157;Q14157-1;Q14157-3;Q14157-4;Q14157-5;Q5VU77;Q5VU78;Q5VU79;Q5VU80;Q5VU81
B4DIZ2	Ubiquitin-conjugating enzyme E2 K (cD FLJ57995, moderately similar to Ubiquitin-conjugating enzyme E2-25 kDa (EC 6.3.2.19))	B4DIZ2;D6RDM7;P61086;P61086-2
P68036	Ubiquitin-conjugating enzyme E2 L3 (EC 6.3.2.19) (L-UBC) (UbcH7) (Ubiquitin carrier protein L3) (Ubiquitin-conjugating enzyme E2-F1) (Ubiquitin-protein ligase L3)	P68036;P68036-2;P68036-3
F8VSD4	Ubiquitin-conjugating enzyme E2 N	F8VSD4;F8VV71;F8VZ29;P61088;Q5JXB2
P22314	Ubiquitin-like modifier-activating enzyme 1 (Protein A1S9) (Ubiquitin-activating enzyme E1)	P22314;Q5JRR6;P22314-2
Q3KQV9	UDP-N-acetylhexosamine pyrophosphorylase-like protein 1 (EC 2.7.7.-)	Q3KQV9
F8W810	Uncharacterized protein	F8W810;H7BZU1;P41091;Q2VIR3;Q2VIR3-2
H3BML4	Uncharacterized protein	H3BML4;H3BRP9;H3BV43;H9KV29;O00241;O00241-2;P78324;P78324-2
B4DUC5	Uncharacterized protein (cD FLJ53202, highly similar to Exportin-2)	B4DUC5;P55060;P55060-3;P55060-4
B4DWJ2	Uncharacterized protein (cD FLJ54314, highly similar to Glutamyl-tR synthetase (EC 6.1.1.18))	B4DWJ2;P47897
Q9UKN7	Unconventional myosin-XV (Unconventional myosin-15)	Q9UKN7
Q969H8	UPF0556 protein C19orf10 (Interleukin-25) (IL-25) (Stromal cell-derived growth factor SF20)	Q969H8
E7EUC7	UTP--glucose-1-phosphate uridylyltransferase	C9JQU9;C9JUW1;C9JWG0;E7EUC7;F2Z3H1;Q16851;Q16851-2;C9JNZ1;C9JTZ5;C9JVG2
K7ELW1	UV excision repair protein RAD23 homolog A	K7ELW1;K7ENJ0;P54725;P54725-2;P54727;Q5W0S4;Q5W0S5;P54725-3
P54727	UV excision repair protein RAD23 homolog B (HR23B) (hHR23B) (XP-C repair-complementing complex 58 kDa protein) (p58)	P54727;Q5W0S4;Q5W0S5
O75436	Vacuolar protein sorting-associated protein 26A (Vesicle protein sorting 26A) (hVPS26)	O75436;O75436-2;S4R3Q6;S4R2Y3
F8VXU5	Vacuolar protein sorting-associated protein 29	F8VXU5;Q05DG7;Q9UBQ0;Q9UBQ0-2
Q96QK1	Vacuolar protein sorting-associated protein 35 (hVPS35) (Maternal-embryonic 3) (Vesicle protein sorting 35)	Q96QK1
P26640	Valine--tRNA ligase (EC 6.1.1.9) (Protein G7a) (Valyl-tRNA synthetase) (ValRS)	P26640
H3BPZ1	Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3	H3BPZ1;H3BS72;Q9P035
Q9P0L0	Vesicle-associated membrane protein-associated protein A (VAMP-A) (VAMP-associated protein A) (VAP-A) (33 kDa VAMP-associated protein) (VAP-33)	Q9P0L0;Q9P0L0-2
E5RK64	Vesicle-associated membrane protein-associated protein B/C	E5RK64;O95292;O95292-2
D6RBV2	Vesicular integral-membrane protein VIP36	D6RBV2;D6RDX1;Q12907;D6RIU4
H0Y394	Vigilin	H0Y394;Q00341;Q00341-2
P08670	Vimentin	P08670

P18206	Vinculin (Metavinculin) (MV)	P18206;P18206-2;Q5JQ13
P21796	Voltage-dependent anion-selective channel protein 1 (VDAC-1) (hVDAC1) (Outer mitochondrial membrane protein porin 1) (Plasmalemmal porin) (Porin 31HL) (Porin 31HM)	P21796
A2A3S1	Voltage-dependent anion-selective channel protein 2	A2A3S1;P45880;P45880-1;P45880-2;Q5JSD1;Q5JSD2
A6NLU5	V-set and transmembrane domain-containing protein 2B	A6NLU5
B7Z1R5	V-type proton ATPase catalytic subunit A#	B7Z1R5;C9JVVW8;P38606;C9JA17
E7EV59	V-type proton ATPase subunit C 1 (V-ATPase subunit C 1) (Vacuolar proton pump subunit C 1)	E7EV59;P21283;Q8NEY4;Q8NEY4-2
G3V2S6	V-type proton ATPase subunit D	G3V2S6;G3V559;H0YJ55;H0YJS0;Q9Y5K8
P36543	V-type proton ATPase subunit E 1 (V-ATPase subunit E 1) (V-ATPase 31 kDa subunit) (p31) (Vacuolar proton pump subunit E 1)	P36543;P36543-3;Q96A05;C9J8H1;P36543-2
Q15904	V-type proton ATPase subunit S1 (V-ATPase subunit S1) (Protein XAP-3) (V-ATPase Ac45 subunit) (V-ATPase S1 accessory protein) (Vacuolar proton pump subunit S1)	Q15904
O75083	WD repeat-containing protein 1 (Actin-interacting protein 1) (AIP1) (NORI-1)	D6RD66;O75083;O75083-3
Q9UNX4	WD repeat-containing protein 3	Q9UNX4
Q96MR6	WD repeat-containing protein 65	Q96MR6
Q6ZMY6	WD repeat-containing protein 88 (PQQ repeat and WD repeat-containing protein)	Q6ZMY6;Q6ZMY6-2
G8JLB2	Xaa-Pro aminopeptidase 1#	G8JLB2;Q5T6H2;Q5T6H7;Q9NQW7;Q9NQW7-2;Q9NQW7-3
P12955	Xaa-Pro dipeptidase (X-Pro dipeptidase) (EC 3.4.13.9) (Imidodipeptidase) (Peptidase D) (Proline dipeptidase) (Prolidase)	P12955;P12955-2;P12955-3
P17040	Zinc finger and SCAN domain-containing protein 20 (Zinc finger protein 31) (Zinc finger protein 360) (Zinc finger protein KOX29)	P17040-4
Q96NC0	Zinc finger matrin-type protein 2	Q96NC0;R4GNG8
Q96KM6	Zinc finger protein 512B	Q96KM6
H3BQQ2	Zinc finger protein 598	H3BQQ2;Q86UK7;Q86UK7-2;Q86UK7-3

Table 2 discloses proteins whose peptides were found to be regulated by at least 60% in in the CSF of AD patients compared to CSF of non-AD subjects. Uniprot ID = annotated ID during data search; Protein names = protein name/s given to matched sequence; All Uniprot matches = All Uniprot IDs that match to the peptide sequence detected at the time of invention. Hash (#) indicates those proteins that were annotated as "merged with ###" and which have been re-searched in Uniprot. Asterisk (*) indicates those proteins which were annotated as deleted as the entry has been removed from Uniprot (due to redundancy).

In one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or

thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, or at least two or more, optionally at least three or all biomarkers selected from the group of Apolipoprotein E, Secretogranin-1, Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform, Cytoplasmic
 5 dynein 1 heavy chain 1, RuvB-like 1, cDNA FLJ54806, Alpha-1-acid glycoprotein 2, Ras-related protein Rab-13, Serum albumin and Pigment epithelium-derived factor.

The biomarker panel may comprise phosphoglucosyltransferase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment
 10 thereof; and at least one, optionally two or more biomarkers selected from Table 1 and/or Table 2 and/or Table 3 or fragments thereof.

Table 3

<u>Uniprot ID</u>	<u>Protein Name</u>	<u>All Uniprot matches</u>
P61981	14-3-3 protein gamma (Protein kinase C inhibitor protein 1) (KCIP-1) [Cleaved into: 14-3-3 protein gamma, N-terminally processed]	P61981
E9PG15	14-3-3 protein theta	E9PG15;P27348
E9PL38	26S proteasome non-ATPase regulatory subunit 13	E9PL38;H0YD73;J3KNQ3;Q9UNM6;Q9UNM6-2
E9PS50	40S ribosomal protein S13	E9PS50;J3KMX5;P62277
P47914	60S ribosomal protein L29 (Cell surface heparin-binding protein HIP)	P47914
P62424	60S ribosomal protein L7a (PLA-X polypeptide) (Surfeit locus protein 3)	P62424;Q5T8U2
E7EMM4	Acid ceramidase	E7EMM4;E7ERV9;Q13510;Q13510-2;Q13510-3
B7Z683	Active breakpoint cluster region-related protein (cDNA FLJ54747, highly similar to Active breakpoint cluster region-related protein)	B7Z683;I3L0R7;Q12979;Q12979-2;Q12979-4
P43652	Afamin (Alpha-albumin) (Alpha-Alb)	P43652
P02763	Alpha-1-acid glycoprotein 1 (AGP 1) (Orosomucoid-1) (OMD 1)	P02763
P19652	Alpha-1-acid glycoprotein 2 (AGP 2) (Orosomucoid-2) (OMD 2)	P19652
G3V3A0	Alpha-1-antichymotrypsin (Serpine peptidase inhibitor, clade A (Alpha-1 antiproteinase, antitrypsin), member 3, isoform CRA_a)	G3V3A0;P01011
P04217	Alpha-1B-glycoprotein (Alpha-1-B glycoprotein)	P04217;P04217-2
P50995	Annexin A11 (56 kDa autoantigen) (Annexin XI) (Annexin-11) (Calcyclin-associated annexin 50) (CAP-50)	P50995-2;P50995
P01008	Antithrombin-III (ATIII) (Serpine C1)	P01008
B3KNW	AP-1 complex subunit gamma-1 (cDNA FLJ30560 fis,	B3KNW1;B3KXW5;J3KQU9;

1	clone BRAWH2004217, highly similar to AP-1 complex subunit gamma-1)	O43747;O43747-2
P02647	Apolipoprotein A-I (Apo-AI) (ApoA-I) (Apolipoprotein A1) [Cleaved into: Proapolipoprotein A-I (ProapoA-I); Truncated apolipoprotein A-I (Apolipoprotein A-I(1-242))]	P02647
P02652	Apolipoprotein A-II (Apo-AII) (ApoA-II) (Apolipoprotein A2) [Cleaved into: Proapolipoprotein A-II (ProapoA-II); Truncated apolipoprotein A-II (Apolipoprotein A-II(1-76))]	P02652;V9GYC1;V9GYG9;V9GYM3;V9GYS1
P06727	Apolipoprotein A-IV (Apo-AIV) (ApoA-IV) (Apolipoprotein A4)	P06727
P04114	Apolipoprotein B-100 (Apo B-100) [Cleaved into: Apolipoprotein B-48 (Apo B-48)]	P04114
B4DG16	Asparagine--tRNA ligase, cytoplasmic#	B4DG16;K7EIU7;K7EJ19;K7EPK2;K7EQ35;O43776
P25705	ATP synthase subunit alpha, mitochondrial	P25705-3;P25705;P25705-2;K7EK77;P25705-3;K7EQH4;K7ERX7;P25705;P25705-2;K7EJP1
C9JHK9	ATP-binding cassette sub-family F member 2	C9JHK9;C9JZV3;Q75MJ1;Q9UG63
B4E3P0	ATP-citrate synthase (cD FLJ55447, highly similar to ATP-citrate synthase (EC 2.3.3.8))	B4E3P0;K7EIE7;P53396;P53396-2
O14497	AT-rich interactive domain-containing protein 1A (ARID domain-containing protein 1A) (B120) (BRG1-associated factor 250) (BAF250) (BRG1-associated factor 250a) (BAF250A) (Osa homolog 1) (hOSA1) (SWI-like protein) (SWI/SNF complex protein p270) (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin subfamily F member 1) (hELD)	O14497;O14497-2
A2A296	BAG family molecular chaperone regulator 2	A2A296;B4DXE2;O95816
P02749	Beta-2-glycoprotein 1 (APC inhibitor) (Activated protein C-binding protein) (Anticardiolipin cofactor) (Apolipoprotein H) (Apo-H) (Beta-2-glycoprotein I) (B2GPI) (Beta(2)GPI)	J3QLI0;J3QRN2;P02748
P07814	Bifunctional glutamate/proline--tR ligase (Bifunctional aminoacyl-tR synthetase) (Cell proliferation-inducing gene 32 protein) (Glutamyl-prolyl-tR synthetase) [Includes: Glutamate--tR ligase (EC 6.1.1.17) (Glutamyl-tR synthetase) (GluRS); Proline--tR ligase (EC 6.1.1.15) (Prolyl-tR synthetase)]	P07814
A6NJ33	Butyrophilin-like protein 9*	A6NJ33;B7Z4Y8;Q6UXG8;Q6UXG8-2;Q6UXG8-3
D6R938	Calcium/calmodulin-dependent protein kinase (CaM kinase) II delta, isoform CRA_e (Calcium/calmodulin-dependent protein kinase type II subunit delta)	D6R938;E9PBG7;E9PF82;H0Y9J2;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9
P27824	Calnexin (IP90) (Major histocompatibility complex class I antigen-binding protein p88) (p90)	P27824-2;P27824
E7EU96	Casein kinase II subunit alpha	E7EU96;P68400;P68400-2;Q8NEV1
B3KXW5	cDNA FLJ46199 fis, clone TEST14007965, highly similar to AP-1 complex subunit gamma-1	B3KXW5;J3KQU9;O43747;O43747-2
B4DIZ2	cDNA FLJ57995, moderately similar to	B4DIZ2;D6RDM7;P61086;P6

	Ubiquitin-conjugating enzyme E2-25 kDa (EC 6.3.2.19)	1086-3
P00450	Ceruloplasmin (EC 1.16.3.1) (Ferroxidase)	H7C5R1;P00450
M0R1L7	Charged multivesicular body protein 2a	M0R1L7;M0R1T5;O43633
F5H5N6	Clathrin heavy chain 2	F5H5N6;J3KR87;J3KS13;J3KSQ2;P53675;P53675-2;Q00610;Q00610-2
P09496	Clathrin light chain A (Lca)	P09496-2;P09496-5
E9PK25	Cofilin-1	P23528;Q9Y281;E9PK25;E9PP50;E9PQB7;F6RFD5;G3V1A4;P60981;P60981-2;Q9Y281-3
P02452	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	P02452
P08572	Collagen alpha-2(IV) chain [Cleaved into: Canstatin]	P08572
P01024	Complement C3 (C3 and PZP-like alpha-2-macroglobulin domain-containing protein 1) [Cleaved into: Complement C3 beta chain; C3-beta-c (C3bc); Complement C3 alpha chain; C3a anaphylatoxin; Acylation stimulating protein (ASP) (C3adesArg); Complement C3b alpha' chain; Complement C3c alpha' chain fragment 1; Complement C3dg fragment; Complement C3g fragment; Complement C3d fragment; Complement C3f fragment; Complement C3c alpha' chain fragment 2]	M0QYC8;P01024
F5GXS0	Complement C4-B	F5GXS0;P0C0L4;P0C0L4-2;P0C0L5
P07357	Complement component C8 alpha chain (Complement component 8 subunit alpha)	P07357
P08603	Complement factor H (H factor 1)	P08603
B1AKG0	Complement factor H-related protein 1	B1AKG0;P08603;Q03591
H3BRY3	Coronin	H3BRY3;P31146
F8W872	Cyclin-dependent kinase 10	F8W872;H3BT74;Q15131;Q15131-2;Q15131-3;Q15131-4
O43175	D-3-phosphoglycerate dehydrogenase (3-PGDH) (EC 1.1.1.95)	O43175;Q5SZU1
B7WPD1	Doublecortin domain-containing protein 1*	B7WPD1;M0R2J8
E7EMD0	DPH--cytochrome P450 reductase	E7EMD0;E7EPN3;E7EVY7;F5H468;H0Y4R2;P16435
P49792	E3 SUMO-protein ligase RanBP2 (EC 6.3.2.-) (358 kDa nucleoporin) (Nuclear pore complex protein Nup358) (Nucleoporin Nup358) (Ran-binding protein 2) (RanBP2) (p270)	P49792
E9PK01	Elongation factor 1-delta	E9PK01;E9PQC9;E9PQZ1;E9PRY8;H0YE58;H0YE72;P29692;P29692-2;P29692-3;P29692-4
P13639	Elongation factor 2 (EF-2)	P13639
E7EQG2	Eukaryotic initiation factor 4A-II	E7EQG2;J3KSN7;J3KT12;J3KTB5;J3QL43;J3QLN6;J3QR64;P60842;P60842-2;Q1424

		0;Q14240-2;J3KS25;J3QKZ9
P05198	Eukaryotic translation initiation factor 2 subunit 1 (Eukaryotic translation initiation factor 2 subunit alpha) (eIF-2-alpha) (eIF-2A) (eIF-2alpha)	P05198
Q8IXL6	Extracellular serine/threonine protein kinase FAM20C (EC 2.7.11.1) (Dentin matrix protein 4) (DMP-4) (Golgi-enriched fraction casein kinase) (GEF-CK) (Protein FAM20C)	Q8IXL6
Q01469	Fatty acid-binding protein, epidermal (Epidermal-type fatty acid-binding protein) (E-FABP) (Fatty acid-binding protein 5) (Psoriasis-associated fatty acid-binding protein homolog) (PA-FABP)	Q01469
G3V0F2	Ferredoxin reductase, isoform CRA_c (DPH:adrenodoxin oxidoreductase, mitochondrial)	G3V0F2;J3QQX3;P22570;P22570-2;P22570-3;P22570-4;P22570-5;P22570-6;P22570-7
E9PPQ4	Ferritin	E9PPQ4;E9PRK8;G3V192;G3V1D1;P02794
D6REL8	Fibrinogen beta chain	D6REL8;P02675
J3KTJ6	Gamma-soluble NSF attachment protein	J3KTJ6;Q99747
B7Z403	Glyoxalase domain-containing protein 4 (cD FLJ55095)	B7Z403;Q9HC38;Q9HC38-2
A8MTJ3	Guanine nucleotide-binding protein G(t) subunit alpha-3 (Gustducin alpha-3 chain)	A8MTJ3;P04899-5;P04899-6;F5GZL8;P04899;P04899-2;P04899-3;P04899-4;P08754;P11488;P19087;P38405-3;P63096;P63096-2
P00739	Haptoglobin-related protein	P00739;P00739-2
Q92598	Heat shock protein 105 kDa (Antigen NY-CO-25) (Heat shock 110 kDa protein)	Q92598-4;Q92598;Q92598-2;Q92598-3;R4GN69
I3L0K7	Heat shock protein 75 kDa, mitochondrial (TNF receptor-associated protein 1, isoform CRA_b)	Q12931-2;I3L0K7;I3L239;Q12931
P68871	Hemoglobin subunit beta (Beta-globin) (Hemoglobin beta chain) [Cleaved into: LVV-hemorphin-7; Spinorphin]	P68871
P02790	Hemopexin (Beta-1B-glycoprotein)	P02790
P61978	Heterogeneous nuclear ribonucleoprotein K (hnRNP K) (Transformation up-regulated nuclear protein) (TUNP)	P61978;P61978-2;P61978-3;Q5T6W1;Q5T6W2;Q5T6W5
B4DT28	Heterogeneous nuclear ribonucleoprotein R (Heterogeneous nuclear ribonucleoprotein R, isoform CRA_a) (cD FLJ54544, highly similar to Heterogeneous nuclear ribonucleoprotein R)	B4DT28;O43390;O43390-2;O43390-3;S4R3J4
P01861	Ig gamma-4 chain C region	P01861
P23083	Ig heavy chain V-I region V35	P23083
F8WAR6	Kinesin-like protein KIF3C	F8WAR6;F8WER6;O14782
Q04760	Lactoylglutathione lyase (EC 4.4.1.5) (Aldoketomutase) (Glyoxalase I) (Glx I) (Ketone-aldehyde mutase) (Methylglyoxalase) (S-D-lactoylglutathione methylglyoxal lyase)	Q04760;Q04760-2
E9PBF6	Lamin-B1	E9PBF6;P20700
Q92615	La-related protein 4B (La ribonucleoprotein domain family member 4B) (La ribonucleoprotein domain family member	Q92615

	5) (La-related protein 5)	
P51884	Lumican (Keratan sulfate proteoglycan lumican) (KSPG lumican)	P51884
F8W6P5	LVV-hemorphin-7	F8W6P5;P68871
Q7Z7M0	Multiple epidermal growth factor-like domains protein 8 (Multiple EGF-like domains protein 8) (Epidermal growth factor-like protein 4) (EGF-like protein 4)	Q7Z7M0;Q7Z7M0-2
B4DYH8	N-acetylglucosamine-6-sulfatase#	B4DYH8;F6S8M0;H0YFA9;H7C3P4;P15586;F5H4C6
O43505	N-acetyllactosaminide beta-1,3-N-acetylglucosaminyltransferase (EC 2.4.1.149) (I-beta-1,3-N-acetylglucosaminyltransferase) (iGnT) (Poly-N-acetyllactosamine extension enzyme) (UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 1)	O43505
Q96PD5	N-acetylmuramoyl-L-alanine amidase (EC 3.5.1.28) (Peptidoglycan recognition protein 2) (Peptidoglycan recognition protein long) (PGRP-L)	Q96PD5;Q96PD5-2
O00567	Nucleolar protein 56 (Nucleolar protein 5A)	O00567;Q5JXT2
H7BY16	Nucleolin	P19338;H7BY16
A8MXH2	Nucleosome assembly protein 1-like 4	A8MXH2;B3KNT8;B3KV44;B7Z9C2;C9J6D1;C9JZI7;E9PJJ2;E9PKT8;E9PNJ7;E9PNW0;E9PS34;F5H4R6;F5H4FY4;F8VRJ2;F8VUX1;F8VV59;F8VVB5;F8VXI6;F8VY35;F8W020;F8W0J6;F8W118;F8W543;H0YH88;H0YHC3;H0YIV4;P55209;Q99733
B4E1F0	Plasma protease C1 inhibitor#	B4E1F0;B4E1H2;E9PGN7;P05155
P00747	Plasminogen (EC 3.4.21.7) [Cleaved into: Plasmin heavy chain A; Activation peptide; Angiostatin; Plasmin heavy chain A, short form; Plasmin light chain B]	P00747
Q15149	Plectin (PCN) (PLTN) (Hemidesmosomal protein 1) (HD1) (Plectin-1)	Q15149;Q15149-2;Q15149-3;Q15149-4;Q15149-5;Q15149-6;Q15149-7;Q15149-8;Q15149-9
O75051	Plexin-A2 (Semaphorin receptor OCT)	O75051
H0YAB0	Prelamin-A/C	H0YAB0;P02545;P02545-2;P02545-3;P02545-4;P02545-5;P02545-6;Q5TCI8
I3L1Q5	Pre-rRNA-processing protein TSR1 homolog	I3L1Q5;Q2NL82
H0Y7L7	Presequence protease, mitochondrial	H0Y7L7;Q5JRX3;Q5JRX3-2;Q5JRX3-3
E9PIF2	Probable ATP-dependent RNA helicase DDX10	E9PIF2;Q13206
B4DLW8	Probable ATP-dependent RNA helicase DDX5#	B4DLW8;C9JMU5;H3BLZ8;J3KRZ1;J3KTA4;J3QRQ7;P17844;Q92841;Q92841-1;Q92841-2;Q92841-3

Q7Z4N8	Prolyl 4-hydroxylase subunit alpha-3 (4-PH alpha-3) (EC 1.14.11.2) (Procollagen-proline,2-oxoglutarate-4-dioxygenase subunit alpha-3)	Q7Z4N8-3
P02760	Protein AMBP [Cleaved into: Alpha-1-microglobulin (Protein HC) (Alpha-1 microglycoprotein) (Complex-forming glycoprotein heterogeneous in charge); Inter-alpha-trypsin inhibitor light chain (ITI-LC) (Bikunin) (EDC1) (HI-30) (Uronic-acid-rich protein); Trypstatin]	P02760;S4R471
K7ER74	Protein APOC4-APOC2	K7ER74;P02655;Q6P163
Q6ZSJ9	Protein shisa-6 homolog	Q6ZSJ9;Q6ZSJ9-2;Q6ZSJ9-3
Q9BVV6-3	Protein TALPID3	Q9BVV6-3
B7Z972	Protein-L-isoaspartate O-methyltransferase (EC 2.1.1.77)	B7Z972;H7BY58;P22061;P22061-2
P59074	Putative charged multivesicular body protein 4B-like protein CHMP4BP1 (Charged multivesicular body protein 4B pseudogene 1)	Q9H444;P59074
O60361	Putative nucleoside diphosphate kinase (NDK) (NDP kinase) (EC 2.7.4.6)	O60361;P22392;P22392-2;Q32Q12
D6RHH8	Rap1 GTPase-GDP dissociation stimulator 1	D6RHZ7;P52306;P52306-2;P52306-3;P52306-4;P52306-5;P52306-6;D6RHH8
P46940	Ras GTPase-activating-like protein IQGAP1 (p195)	P46940
E7END7	Ras-related protein Rab-1A	E7END7;P62820
P62834	Ras-related protein Rap-1A (C21KG) (G-22K) (GTP-binding protein smg p21A) (Ras-related protein Krev-1)	P62834
E7ENU7	Ribosomal protein L15	E7ENU7;E7EQV9;E7EX53;P61313;P61313-2
B3KQ59	RuvB-like 2#	B3KQ59;M0R0Y3;Q9Y230
F8VZQ9	SAP domain-containing ribonucleoprotein	F8VZQ9;H0YHG0;P82979;Q567R9
B5MCX3	Septin-2	B5MCX3;H7C2Y0;Q15019;Q15019-2;Q15019-3
J3KN47	Serotransferrin*	J3KN47;P02787
B7WNR0	Serum albumin	B7WNR0;C9JKR2;D6RHD5;H0YA55;P02768;P02768-2
F5H4W9	Serum paraoxonase/arylesterase 1*	F5H4W9;P27169
F8WF42	Serum paraoxonase/arylesterase 1	F8WF42;P27169
B0FWH5	Sex hormone binding globulin (Sex hormone-binding globulin)	B0FWH5;B0FWH6;B0FWH7;B4DYU0;I3L0M1;I3L145;I3L1C1;I3L1G4;I3L1J1;I3L2F1;I3L2X4;I3L4B9;P04278;P04278-2;P04278-3;P04278-4;P04278-5
G3V2B	Short peptide from AAT	G3V2B9;P01009;P01009-2;P

9		01009-3
A6NKH 4	Sorting nexin-1*	A6NKH4;H0YK42;Q13596;Q13596-2;Q13596-3
Q15459	Splicing factor 3A subunit 1 (SF3a120) (Spliceosome-associated protein 114) (SAP 114)	Q15459-2;Q15459
D6RFM 5	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	D6RFM5;P31040-2;P31040;P31040-3
F5GXC 8	Succinyl-CoA ligase [ADP-forming] subunit beta, mitochondrial*	F5GXC8;Q5T9Q5;Q9P2R7;Q9P2R7-2
Q5TCU 6	Talin-1	Q9Y490;Q5TCU6;Q9Y4G6
B7ZAR 1	T-complex protein 1 subunit epsilon (cDNA, FLJ79275, highly similar to T-complex protein 1 subunit epsilon)	P48643-2;B7ZAR1;E7ENZ3;E9PCA1;P48643
B4DUR 8	T-complex protein 1 subunit gamma (cD FLJ57603, highly similar to T-complex protein 1 subunit gamma) (cD, FLJ78822, highly similar to T-complex protein 1 subunit gamma) (cD, FLJ79286, highly similar to T-complex protein 1 subunit gamma)	B4DUR8;E9PRC8;P49368;Q5SZX6;Q5SZX9
E9PHK 0	Tetranectin	E9PHK0;P05452
E7EQ7 2	Transmembrane emp24 domain-containing protein 2	E7EQ72;F5GX39;Q15363
K7EJI9	Truncated apolipoprotein C-I	K7EJI9;K7ELM9;K7EPF9;K7ERI9;P02654;K7EKP1
G3V2J9	Tubulin polyglutamylase TTLL5	G3V2J9;Q6EMB2;Q6EMB2-3
Q9UIG0	Tyrosine-protein kinase BAZ1B (EC 2.7.10.2) (Bromodomain adjacent to zinc finger domain protein 1B) (Williams syndrome transcription factor) (Williams-Beuren syndrome chromosomal region 10 protein) (Williams-Beuren syndrome chromosomal region 9 protein) (hWALp2)	Q9UIG0;Q9UIG0-2
B4E1Z4	Uncharacterized protein (cDNA FLJ55673, highly similar to Complement factor B (EC 3.4.21.47))	B4E1Z4;E7ETN3;H7C5H1;P00751
H0Y426	Valine--tRNA ligase	H0Y426;P26640
C9J8H1	V-type proton ATPase subunit E 1	C9J8H1;P36543;P36543-2;P36543-3
E9PB87	WAS/WASL-interacting protein family member 1	E9PB87;O43516;O43516-2;O43516-3
Q06732	Zinc finger protein 33B (Zinc finger protein 11B) (Zinc finger protein KOX2)	Q32M84;Q32M84-2;Q06732
C9JEV0	Zinc-alpha-2-glycoprotein	C9JEV0;P25311

Table 3 discloses proteins whose peptides were found to be down-regulated by at least 60% in in the CSF of AD patients compared to CSF of non-AD subjects. Uniprot ID = annotated ID during data search; Protein names = protein name/s given to matched sequence; All Uniprot matches = All Uniprot IDs that match to the peptide sequence detected at the time of invention. Hash (#) indicates those proteins that were annotated as "merged with ###" and which have been re-searched in Uniprot. Asterisk (*) indicates those proteins which were annotated as deleted as the entry has been removed from Uniprot (due to redundancy).

In one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, or at least two or more, optionally at least three or all

5 biomarkers selected from the group of ubiquitin carboxy-terminal hydrolase L1, vitamin D binding protein Peroxiredoxin-1, MARCKS-related protein, Moesin, Actin, Protein TMSB4XP4, ApoE, Gelsolin, Secretogranin, Albumin and complement proteins, Apolipoprotein E, Secretogranin-1, Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform, Cytoplasmic dynein 1 heavy chain 1, RuvB-like 1, cDNA FLJ54806, Alpha-1-acid glycoprotein 2, Ras-related

10 protein Rab-13, Serum albumin and Pigment epithelium-derived factor or fragments thereof.

The biomarker panel may comprise phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, optionally two or more biomarkers selected from Table 1 and/or Table 2

15 and/or Table 3 and/or Table 4 or fragments thereof.

Table 4

<u>Uniprot ID</u>	<u>Protein Name</u>	<u>All Uniprot matches</u>
I3L0S5	76 kDa lysosomal alpha-glucosidase	I3L0S5;I3L3L3;P10253
P42684	Abelson tyrosine-protein kinase 2 (EC 2.7.10.2) (Abelson murine leukemia viral oncogene homolog 2) (Abelson-related gene protein) (Tyrosine-protein kinase ARG)	P42684;P42684-10;P42684-2;P42684-3;P42684-4;P42684-5;P42684-6;P42684-7;P42684-8
G5E951	ADAM metallopeptidase domain 22, isoform CRA_I (Disintegrin and metalloproteinase domain-containing protein 22)	E7EPF1;F8WAD8;G5E951;Q9P0K1;Q9P0K1-2;Q9P0K1-3;Q9P0K1-4;Q9P0K1-5
Q9UKB5	Adherens junction-associated protein 1 (Membrane protein shrew-1)	Q9UKB5
Q12955	Ankyrin-3 (ANK-3) (Ankyrin-G)	Q12955;Q12955-4;Q12955-5
Q6P163	APOC2 protein (Apolipoprotein C-II)	P02655;K7ER74;Q6P163
P02654	Apolipoprotein C-I (Apolipoprotein C1) [Cleaved into: Truncated apolipoprotein C-I]	K7EJI9;K7ELM9;K7EPF9;K7ERI9;P02654
P02655	Apolipoprotein C-II (Apo-CII) (ApoC-II) (Apolipoprotein C2)	P02655;K7ER74
P02656	Apolipoprotein C-III (Apo-CIII) (ApoC-III) (Apolipoprotein C3)	P02656;B0YIW2
P17174	Aspartate aminotransferase, cytoplasmic (cAspAT) (EC 2.6.1.1) (EC 2.6.1.3) (Cysteine aminotransferase, cytoplasmic) (Cysteine transaminase, cytoplasmic) (cCAT) (Glutamate oxaloacetate transaminase 1) (Transaminase A)	P17174;B7Z7E9
P35613	Basigin (5F7) (Collagenase stimulatory factor) (Extracellular matrix metalloproteinase inducer)	P35613;P35613-2;P35613-3;P35613-4

	(EMMPRIN) (Leukocyte activation antigen M6) (OK blood group antigen) (Tumor cell-derived collagenase stimulatory factor) (TCSF) (CD antigen CD147)	
Q96JF0	Beta-galactoside alpha-2,6-sialyltransferase 2 (Alpha 2,6-ST 2) (EC 2.4.99.1) (CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,6-sialyltransferase 2) (ST6Gal II) (ST6GalIII) (hST6Gal II) (Sialyltransferase 2)	Q96JF0;Q96JF0-2
H3BP20	Beta-hexosaminidase (EC 3.2.1.52)	E9PGL4;H3BP20;H3BS10;P06865
P06865	Beta-hexosaminidase subunit alpha (EC 3.2.1.52) (Beta-N-acetylhexosaminidase subunit alpha) (Hexosaminidase subunit A) (N-acetyl-beta-glucosaminidase subunit alpha)	E9PGL4;H3BP20;H3BS10;P06865
A2A3C1	Brain-specific angiogenesis inhibitor 2	A2A3C1;A2A3C2;A2A3C3;A2A3C4;A2A3C6;E9PND1;O60241;O60241-2;O60241-3;O60241-4
Q32M84	BTB/POZ domain-containing protein 16	Q06732;Q32M84;Q32M84-2
Q9HCU4	Cadherin EGF LAG seven-pass G-type receptor 2 (Cadherin family member 10) (Epidermal growth factor-like protein 2) (EGF-like protein 2) (Fleming homolog 3) (Multiple epidermal growth factor-like domains protein 3) (Multiple EGF-like domains protein 3)	Q9HCU4
Q5SWX3	Calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma, isoform CRA_n (Calcium/calmodulin-dependent protein kinase type II subunit gamma)	Q9Y266;B7Z1Z6;D6R938;E9PBG7;E9PF82;H0Y6G2;H0Y9C2;H0Y9J2;H7C394;Q13217;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
Q6P2M8	Calcium/calmodulin-dependent protein kinase type 1B (EC 2.7.11.17) (CaM kinase I beta) (CaM kinase IB) (CaM-KI beta) (CaMKI-beta) (Pregnancy up-regulated non-ubiquitously-expressed CaM kinase)	Q6P2M8;Q6P2M8-2;Q6P2M8-3;Q6P2M8-5;Q6P2M8-6
Q9UQM7	Calcium/calmodulin-dependent protein kinase type II subunit alpha (CaM kinase II subunit alpha) (CaMK-II subunit alpha) (EC 2.7.11.17)	Q9Y266;B7Z1Z6;D6R938;E9PBG7;E9PF82;H0Y6G2;H0Y9C2;H0Y9J2;H7C394;Q13217;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
Q13554	Calcium/calmodulin-dependent protein kinase type II subunit beta (CaM kinase II subunit beta) (CaMK-II subunit beta) (EC 2.7.11.17)	Q9Y266;B7Z1Z6;D6R938;E9PBG7;E9PF82;H0Y6G2;H0Y9C2;H0Y9J2;H7C394;Q13217;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13

		557-6;Q13557-8;Q13557-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
Q13555	Calcium/calmodulin-dependent protein kinase type II subunit gamma (CaM kinase II subunit gamma) (CaMK-II subunit gamma) (EC 2.7.11.17)	Q9Y266;B7Z1Z6;D6R938;E9PBG7;E9PF82;H0Y6G2;H0Y9C2;H0Y9J2;H7C394;Q13217;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q13557;Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
Q9BQT9	Calsyntenin-3 (Alcadein-beta) (Alc-beta)	Q9BQT9;Q9BQT9-2
Q5T8F0	Cathepsin L1	P07711;Q5T8F0
P25774	Cathepsin S (EC 3.4.22.27)	P25774;P25774-2;U3KQE7
Q8N3J6	Cell adhesion molecule 2 (Immunoglobulin superfamily member 4D) (IgSF4D) (Nectin-like protein 3) (NECL-3) (Synaptic cell adhesion molecule 2) (SynCAM 2)	Q8N3J6;Q8N3J6-2;Q8N3J6-3
Q8N126	Cell adhesion molecule 3 (Brain immunoglobulin receptor) (Immunoglobulin superfamily member 4B) (IgSF4B) (Nectin-like protein 1) (NECL-1) (Synaptic cell adhesion molecule 3) (SynCAM3) (TSLC1-like protein 1) (TSL1)	Q8N126;Q8N126-2;Q8N126-3
G3V2Y8	Cerebellin-3 (HCG40197)	G3V2Y8;Q6UW01
Q9NTU7	Cerebellin-4 (Cerebellin-like glycoprotein 1)	Q9NTU7
C9J0A7	Charged multivesicular body protein 2b	C9J0A7
P06307	Cholecystokinin (CCK) [Cleaved into: Cholecystokinin-58 (CCK58); Cholecystokinin-58 desnonopeptide ((1-49)-CCK58); Cholecystokinin-39 (CCK39); Cholecystokinin-33 (CCK33); Cholecystokinin-25 (CCK25); Cholecystokinin-18 (CCK18); Cholecystokinin-12 (CCK12); Cholecystokinin-8 (CCK8); Cholecystokinin-7 (CCK7); Cholecystokinin-5 (CCK5)]	P06307
Q16568	Cocaine- and amphetamine-regulated transcript protein [Cleaved into: CART(1-39); CART(42-89)]	Q16568
Q9BXJ4	Complement C1q tumor necrosis factor-related protein 3 (Collagenous repeat-containing sequence 26 kDa protein) (CORS26) (Secretory protein CORS26)	E9PGA6;Q9BXJ4;Q9BXJ4-2;Q9BXJ4-3
Q9C0A0	Contactin-associated protein-like 4 (Cell recognition molecule Caspr4)	E9PDN6;F5H107;Q9C0A0;Q9C0A0-2
Q9UBP4	Dickkopf-related protein 3 (Dickkopf-3) (Dkk-3) (hDkk-3)	F6SYF8;Q9UBP4
Q9P0K1	Disintegrin and metalloproteinase domain-containing protein 22 (ADAM 22) (Metalloproteinase-disintegrin ADAM22-3) (Metalloproteinase-like, disintegrin-like, and cysteine-rich protein 2)	E7EPF1;F8WAD8;G5E951;Q9P0K1;Q9P0K1-2;Q9P0K1-3;Q9P0K1-4;Q9P0K1-5
Q9UJA3	DNA helicase MCM8 (EC 3.6.4.12) (Minichromosome maintenance 8)	Q9UJA3;Q9UJA3-2;Q9UJA3-3;Q9UJA3-4
Q13217	DnaJ homolog subfamily C member 3 (Endoplasmic reticulum DNA J domain-containing protein 6) (ER-resident protein ERdj6) (ERdj6) (Interferon-induced, double-stranded RNA-activated protein kinase inhibitor) (Protein kinase inhibitor of 58 kDa) (Protein kinase inhibitor p58)	Q9Y266;B7Z1Z6;D6R938;E9PBG7;E9PF82;H0Y6G2;H0Y9C2;H0Y9J2;H7C394;Q13217;Q13554;Q13554-2;Q13554-3;Q13554-4;Q13554-5;Q13554-6;Q13554-7;Q13554-8;Q13555;Q13555-10;Q13555-2;Q13555-3;Q13555-4;Q13555-5;Q13555-6;Q13555-7;Q13555-8;Q13555-9;Q13557;

		Q13557-10;Q13557-11;Q13557-12;Q13557-3;Q13557-4;Q13557-5;Q13557-6;Q13557-8;Q13557-9;Q5SWX3;Q8WU40;Q9UQM7;Q9UQM7-2
Q9P225	Dynein heavy chain 2, axonemal (Axonemal beta dynein heavy chain 2) (Ciliary dynein heavy chain 2) (Dynein heavy chain domain-containing protein 3)	P10645;Q9P225;Q9P225-2;Q9P225-3;O60741;Q9P1Z3;Q9UL51;Q9Y3Q4
J3KQG3	EPH receptor A10, isoform CRA_b (Ephrin type-A receptor 10)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
Q6NVW1	EPHB2 protein (Ephrin type-B receptor 2)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
Q5JZY3	Ephrin type-A receptor 10 (EC 2.7.10.1)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
P54764	Ephrin type-A receptor 4 (EC 2.7.10.1) (EPH-like kinase 8) (EK8) (hEK8) (Tyrosine-protein kinase TYRO1) (Tyrosine-protein kinase receptor SEK)	B7Z6Q8;E9PG71;P54764
P54756	Ephrin type-A receptor 5 (EC 2.7.10.1) (Brain-specific kinase) (EPH homology kinase 1) (EHK-1) (EPH-like kinase 7) (EK7) (hEK7)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
Q15375	Ephrin type-A receptor 7 (EC 2.7.10.1) (EPH homology kinase 3) (EHK-3) (EPH-like kinase 11) (EK11) (hEK11)	Q15375;Q15375-2;Q15375-4;Q15375-5
P29322	Ephrin type-A receptor 8 (EC 2.7.10.1) (EPH- and ELK-related kinase) (EPH-like kinase 3) (EK3) (hEK3) (Tyrosine-protein kinase receptor EEK)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
P29323	Ephrin type-B receptor 2 (EC 2.7.10.1) (Developmentally-regulated Eph-related tyrosine kinase) (ELK-related tyrosine kinase) (EPH tyrosine kinase 3) (EPH-like kinase 5) (EK5) (hEK5) (Renal carcinoma antigen NY-REN-47) (Tyrosine-protein kinase TYRO5) (Tyrosine-protein kinase receptor EPH-3)	F8VP57;F8W9W0;J3KQG3;P29322;P29322-2;P54756;P54756-2;P54756-3;Q15375;Q15375-2;Q15375-3;Q15375-4;Q15375-5;Q5JZY3;Q5JZY3-2;Q5JZY3-3;B1AKC9;P29323;P29323-2;P29323-3;Q6NVW1
P52797	Ephrin-A3 (EFL-2) (EHK1 ligand) (EHK1-L) (EPH-related receptor tyrosine kinase ligand 3) (LERK-3)	B4DXG7;P52797
B4DXG7	Ephrin-A3 (Uncharacterized protein) (cDNA FLJ57652, highly similar to Ephrin-A3)	B4DXG7;P52797
P52799	Ephrin-B2 (EPH-related receptor tyrosine kinase ligand 5) (LERK-5) (HTK ligand) (HTK-L)	P52799
Q9UBQ6	Exostosin-like 2 (EC 2.4.1.223) (Alpha-1,4-N-acetylhexosaminyltransferase EXTL2) (Alpha-GalNAcT EXTL2) (EXT-related protein 2) (Glucuronyl-galactosyl-proteoglycan 4-alpha-N-acetylglucosaminyltransferase) [Cleaved into: Processed exostosin-like 2]	C9JEG3;F5GZK1;Q9UBQ6

J3KNT4	Fibroblast growth factor receptor (EC 2.7.10.1)	E7EU09;J3KNT4;P11362;P11362-10;P11362-11;P11362-12;P11362-13;P11362-14;P11362-16;P11362-18;P11362-19;P11362-2;P11362-20;P11362-21;P11362-3;P11362-4;P11362-5;P11362-6;P11362-7;P11362-8;P11362-9;E9PNM3;E9PKF2;E9PKV7;E9PN14
P11362	Fibroblast growth factor receptor 1 (FGFR-1) (EC 2.7.10.1) (Basic fibroblast growth factor receptor 1) (BFGFR) (bFGF-R-1) (Fms-like tyrosine kinase 2) (FLT-2) (N-sam) (Proto-oncogene c-Fgr) (CD antigen CD331)	E7EU09;J3KNT4;P11362;P11362-10;P11362-11;P11362-12;P11362-13;P11362-14;P11362-16;P11362-18;P11362-19;P11362-2;P11362-20;P11362-21;P11362-3;P11362-4;P11362-5;P11362-6;P11362-7;P11362-8;P11362-9;E9PNM3;E9PKF2;E9PKV7;E9PN14
Q6MZW2	Follistatin-related protein 4 (Follistatin-like protein 4)	Q6MZW2;Q6MZW2-3
O00451	GNDF family receptor alpha-2 (GNDF receptor alpha-2) (GDNFR-alpha-2) (GFR-alpha-2) (GNDF receptor beta) (GDNFR-beta) (Neurturin receptor alpha) (NRTNR-alpha) (NTNR-alpha) (RET ligand 2) (TGF-beta-related neurotrophic factor receptor 2)	E5RGR6;O00451;O00451-2;O00451-3
P14314	Glucosidase 2 subunit beta (80K-H protein) (Glucosidase II subunit beta) (Protein kinase C substrate 60.1 kDa protein heavy chain) (PKCSH)	K7ELL7;P14314;P14314-2
Q16769	Glutaminyl-peptide cyclotransferase (EC 2.3.2.5) (Glutaminyl cyclase) (QC) (sQC) (Glutaminyl-tRNA cyclotransferase) (Glutamyl cyclase) (EC)	Q16769
B4DK85	Glutaryl-CoA dehydrogenase, mitochondrial (cDNA FLJ59559, highly similar to Glutaryl-CoA dehydrogenase, mitochondrial (EC 1.3.99.7))	B4DK85;K7ESA6;Q92947;Q92947-2;P13521
Q5VW52	Glycerol-3-phosphate acyltransferase 1, mitochondrial (Glycerol-3-phosphate acyltransferase, mitochondrial, isoform CRA_a)	Q5VW52;Q9HCL2
O60812	Heterogeneous nuclear ribonucleoprotein C-like 1 (hnRNP C-like-1) (hnRNP core protein C-like 1)	O60812
P04233	HLA class II histocompatibility antigen gamma chain (HLA-DR antigens-associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD antigen CD74)	H0YBZ2;P04233
Q86YZ3	Hornerin	Q86YZ3
Q9Y4L1	Hypoxia up-regulated protein 1 (150 kDa oxygen-regulated protein) (ORP-150) (170 kDa glucose-regulated protein) (GRP-170)	E9PL22;Q9Y4L1
P22304	Iduronate 2-sulfatase (EC 3.1.6.13) (Alpha-L-iduronate sulfate sulfatase) (Idursulfase) [Cleaved into: Iduronate 2-sulfatase 42 kDa chain; Iduronate 2-sulfatase 14 kDa chain]	P22304;P22304-2;P22304-3
P04433	Ig kappa chain V-III region VG	P04433
P06316	Ig lambda chain V-I region BL2	P01702;P06316
P01702	Ig lambda chain V-I region NIG-64	P01702;P06316
P04220	Ig mu heavy chain disease protein (BOT)	P04220
B9A064	Immunoglobulin lambda-like polypeptide 5 (G lambda-1) (Germline immunoglobulin lambda 1)	B9A064;P0CG05
Q15111	Inactive phospholipase C-like protein 1 (PLC-L1) (Phospholipase C-deleted in lung carcinoma)	H3BUD4;Q15111;Q15111-2

	(Phospholipase C-related but catalytically inactive protein) (PRIP)	
Q9UMF0	Intercellular adhesion molecule 5 (ICAM-5) (Telencephalin)	Q9UMF0
P01579	Interferon gamma (IFN-gamma) (Immune interferon)	P01579;P14618;P14618-2
Q9NS87	Kinesin-like protein KIF15 (Kinesin-like protein 2) (hKLP2) (Kinesin-like protein 7) (Serologically defined breast cancer antigen NY-BR-62)	C9JKA9;Q9NS87;Q9NS87-2;Q9NS87-3;Q9NS87-4
P24043	Laminin subunit alpha-2 (Laminin M chain) (Laminin-12 subunit alpha) (Laminin-2 subunit alpha) (Laminin-4 subunit alpha) (Merosin heavy chain)	P24043
Q8N2S1	Latent-transforming growth factor beta-binding protein 4 (LTBP-4)	E7EUV1;Q8N2S1-2;Q8N2S1;E7EN G9;F5GXC9;M0QZX0;Q8N2S1-3
O94910	Latrophilin-1 (Calcium-independent alpha-latrotoxin receptor 1) (CIRL-1) (Lectomedin-2)	O94910;O94910-2
P07195	L-lactate dehydrogenase B chain (LDH-B) (EC 1.1.1.27) (LDH heart subunit) (LDH-H) (Renal carcinoma antigen NY-REN-46)	P07195
P10253	Lysosomal alpha-glucosidase (EC 3.2.1.20) (Acid maltase) (Aglucosidase alfa) [Cleaved into: 76 kDa lysosomal alpha-glucosidase; 70 kDa lysosomal alpha-glucosidase]	I3L0S5;I3L3L3;P10253
E9PGC8	MAP1 light chain LC2	E9PGC8;J3KPX8;P78559;P78559-2
Q8TBP5	Membrane protein FAM174A (Hepatitis C virus NS5A-transactivated protein 6) (HCV NS5A-transactivated protein 6) (Transmembrane protein 157)	Q8TBP5
P04731	Metallothionein-1A (MT-1A) (Metallothionein-IA) (MT-IA)	H3BSF1;P02795;P04731;P13640;P13640-2;P80294;P80297
H3BSF1	Metallothionein-1G	H3BSF1;P02795;P04731;P13640;P13640-2;P80294;P80297
P80294	Metallothionein-1H (MT-1H) (Metallothionein-0) (MT-0) (Metallothionein-IH) (MT-IH)	H3BSF1;P02795;P04731;P13640;P13640-2;P80294;P80297
P78559	Microtubule-associated protein 1A (MAP-1A) (Proliferation-related protein p80) [Cleaved into: MAP1A heavy chain; MAP1 light chain LC2]	E9PGC8;J3KPX8;P78559;P78559-2
H0Y786	Nebulin	P20929;F8WCL5;F8WCP0;H0Y786;J3QK84
Q9NQX5	Neural proliferation differentiation and control protein 1 (NPDC-1)	Q5SPY9;Q9NQX5
O14594	Neurocan core protein (Chondroitin sulfate proteoglycan 3)	O14594
Q9BYT8	Neurolysin, mitochondrial (EC 3.4.24.16) (Angiotensin-binding protein) (Microsomal endopeptidase) (MEP) (Mitochondrial oligopeptidase M) (Neurotensin endopeptidase)	E9PCB6;H0YAK4;Q9BYT8
P17677	Neuromodulin (Axonal membrane protein GAP-43) (Growth-associated protein 43) (Neural phosphoprotein B-50) (pp46)	P17677;P17677-2
P47972	Neuronal pentraxin-2 (NP2) (Neuronal pentraxin II) (NP-II)	P47972
Q99574	Neuroserpin (Peptidase inhibitor 12) (PI-12) (Serpine I1)	Q99574;C9JDY5;C9JQU9
P14543	Nidogen-1 (NID-1) (Entactin)	P14543;P14543-2
Q7Z6G3	N-terminal EF-hand calcium-binding protein 2 (EF-hand calcium-binding protein 2) (Neuronal calcium-binding	H3BPH6;H3BTW2;Q7Z6G3

	protein 2) (Synaptotagmin-interacting protein 2) (Stip-2)	
Q5VST9	Obscurin (EC 2.7.11.1) (Obscurin-RhoGEF) (Obscurin-myosin light chain kinase) (Obscurin-MLCK)	P01009;A6NGQ3;F8W8T3;H3BPX2;H3BQA7;H7BY31;Q5VST9;Q5VST9-2;Q5VST9-3;Q5VST9-5;Q5VST9-6
Q96CV9	Optineurin (E3-14.7K-interacting protein) (FIP-2) (Huntingtin yeast partner L) (Huntingtin-interacting protein 7) (HIP-7) (Huntingtin-interacting protein L) (NEMO-related protein) (Optic neuropathy-inducing protein) (Transcription factor IIIA-interacting protein) (TFIIIA-IntP)	P06727;Q96CV9;Q96CV9-2;Q96CV9-3
G5E956	Outer dense fiber of sperm tails 2-like, isoform CRA_a (Outer dense fiber protein 2-like)	G5E956;H0YD68;Q9ULJ1;Q9ULJ1-2;Q9ULJ1-3;Q9ULJ1-4;Q9ULJ1-5;Q9ULJ1-6
H0YD68	Outer dense fiber protein 2-like	G5E956;H0YD68;Q9ULJ1;Q9ULJ1-2;Q9ULJ1-3;Q9ULJ1-4;Q9ULJ1-5;Q9ULJ1-6
H3BUD4	Phosphoinositide phospholipase C (EC 3.1.4.11)	H3BUD4;Q15111;Q15111-2
Q8IV08	Phospholipase D3 (PLD 3) (EC 3.1.4.4) (Choline phosphatase 3) (HindIII K4L homolog) (Hu-K4) (Phosphatidylcholine-hydrolyzing phospholipase D3)	E2QRG1;M0R1F7;M0R2W7;Q8IV08
Q9BTY2	Plasma alpha-L-fucosidase (EC 3.2.1.51) (Alpha-L-fucoside fucohydrolase 2) (Alpha-L-fucosidase 2)	Q9BTY2
O60741	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 1 (Brain cyclic nucleotide-gated channel 1) (BCNG-1)	P10645;Q9P225;Q9P225-2;Q9P225-3;O60741;Q9P1Z3;Q9UL51;Q9Y3Q4
Q9UL51	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 2 (Brain cyclic nucleotide-gated channel 2) (BCNG-2)	P10645;Q9P225;Q9P225-2;Q9P225-3;O60741;Q9P1Z3;Q9UL51;Q9Y3Q4
Q9P1Z3	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 3	P10645;Q9P225;Q9P225-2;Q9P225-3;O60741;Q9P1Z3;Q9UL51;Q9Y3Q4
Q9Y3Q4	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 4	P10645;Q9P225;Q9P225-2;Q9P225-3;O60741;Q9P1Z3;Q9UL51;Q9Y3Q4
E7EQY3	Pregnancy-specific beta-1-glycoprotein 5	E7EQY3;P11464-4
A4D1T9	Probable inactive serine protease 37 (Probable inactive trypsin-X2)	A4D1T9
P09668	Pro-cathepsin H [Cleaved into: Cathepsin H mini chain; Cathepsin H (EC 3.4.22.16); Cathepsin H heavy chain; Cathepsin H light chain]	P09668
F5GZK1	Processed exostosin-like 2	C9JEG3;F5GZK1;Q9UBQ6
P51888	Prolargin (Proline-arginine-rich end leucine-rich repeat protein)	P51888
Q5FWE3	Proline-rich transmembrane protein 3	Q5FWE3;Q5FWE3-3
P01303	Pro-neuropeptide Y [Cleaved into: Neuropeptide Y (Neuropeptide tyrosine) (NPY); C-flanking peptide of NPY (CPON)]	P01303
P48745	Protein NOV homolog (NovH) (CCN family member 3) (Insulin-like growth factor-binding protein 9) (IBP-9) (IGF-binding protein 9) (IGFBP-9) (Nephroblastoma-overexpressed gene protein homolog)	P48745
G3XAD5	Protein tyrosine phosphatase, receptor type, D, isoform CRA_c (Receptor-type tyrosine-protein phosphatase delta)	F5GWR7;F5GWT7;F5GWY7;G3XAD5;G3XAE2;P23468;P23468-2;P23468-3;P23468-4;P23468-5;P23468-6

G3XAE2	Protein tyrosine phosphatase, receptor type, D, isoform CRA_f (Receptor-type tyrosine-protein phosphatase delta)	F5GWR7;F5GWT7;F5GWY7;G3XAD5;G3XAE2;P23468;P23468-2;P23468-3;P23468-4;P23468-5;P23468-6
F5GWR7	Receptor-type tyrosine-protein phosphatase delta	F5GWR7;F5GWT7;F5GWY7;G3XAD5;G3XAE2;P23468;P23468-2;P23468-3;P23468-4;P23468-5;P23468-6
P23470	Receptor-type tyrosine-protein phosphatase gamma (Protein-tyrosine phosphatase gamma) (R-PTP-gamma) (EC 3.1.3.48)	P23470;P23470-2
Q92932	Receptor-type tyrosine-protein phosphatase N2 (R-PTP-N2) (EC 3.1.3.48) (Islet cell autoantigen-related protein) (IAR) (ICAAR) (Phogrin)	E7EM83;Q92932;Q92932-2;Q92932-3;Q92932-4
Q96B86	Repulsive guidance molecule A (RGM domain family member A)	F5GZU6;F5H7G2;G3V518;Q96B86;Q96B86-2
G3V1D7	Reticulon 4 receptor-like 2, isoform CRA_a (Reticulon-4 receptor-like 2)	G3V1D7;Q86UN3;Q86UN3-2
Q9BZR6	Reticulon-4 receptor (Nogo receptor) (NgR) (Nogo-66 receptor)	H7C0V4;H7C215;Q9BZR6
Q6P5S7	Ribonuclease kappa (RNase K) (RNase kappa) (EC 3.1.-.-)	F8W1G5;H0YHM1;H0YIM4;H0YIU3;I3L285;Q6P5S7
Q99985	Semaphorin-3C (Semaphorin-E) (Sema E)	F5H1Z7;Q99985
Q6P3R8	Serine/threonine-protein kinase Nek5 (EC 2.7.11.1) (Never in mitosis A-related kinase 5) (NimA-related protein kinase 5)	E9PIX7;Q6P3R8
E9PQD6	Serum amyloid A protein	E9PQD6;E9PR14;G3V1D9;P0DJI8;P0DJI9;P0DJI9-2
P0DJI8	Serum amyloid A-1 protein (SAA) [Cleaved into: Amyloid protein A (Amyloid fibril protein AA); Serum amyloid protein A(2-104); Serum amyloid protein A(3-104); Serum amyloid protein A(2-103); Serum amyloid protein A(2-102); Serum amyloid protein A(4-101)]	E9PQD6;E9PR14;G3V1D9;P0DJI8;P0DJI9;P0DJI9-2
P0DJI9	Serum amyloid A-2 protein (SAA2)	E9PQD6;E9PR14;G3V1D9;P0DJI8;P0DJI9;P0DJI9-2
Q5TFQ8	Signal-regulatory protein beta-1 isoform 3 (SIRP-beta-1 isoform 3)	P78324;P78324-2;P78324-4;Q5TFQ8
Q8WVQ1	Soluble calcium-activated nucleotidase 1 (SCAN-1) (EC 3.6.1.6) (Apyrase homolog) (Putative MAPK-activating protein PM09) (Putative NF-kappa-B-activating protein 107)	K7EN15;Q8WVQ1;Q8WVQ1-2
A8MXT8	Sulfhydryl oxidase 1	O00391;O00391-2;A8MXT8
H7C2K7	Sushi domain-containing protein 5	H7C2K7;O60279
Q92752	Tenascin-R (TN-R) (Janusin) (Restrictin)	Q92752;Q92752-2
D6RAM7	Testican-1	D6RAM7;Q08629
Q03167	Transforming growth factor beta receptor type 3 (TGF-beta receptor type 3) (TGFR-3) (Betaglycan) (Transforming growth factor beta receptor III) (TGF-beta receptor type III)	E9PKY4;Q03167;Q03167-2
Q3YBM2	Transmembrane protein 176B (Protein LR8)	Q3YBM2;Q3YBM2-2
O95407	Tumor necrosis factor receptor superfamily member 6B (Decoy receptor 3) (DcR3) (Decoy receptor for Fas ligand) (M68)	Q06481;O95407;Q06481-3;Q06481-6
P30530	Tyrosine-protein kinase receptor UFO (EC 2.7.10.1) (AXL oncogene)	P30530;P30530-2

F5H7E1	Uncharacterized protein	P19827;F5H7E1
E9PGA6	Uncharacterized protein	E9PGA6;Q9BXJ4;Q9BXJ4-2;Q9BXJ4-3
M0QY22	Uncharacterized protein	M0QY22
C9JPP7	Uncharacterized protein C1orf87	C9JPP7;Q8N0U7;Q8N0U7-2;Q8N0U7-3
Q13459	Unconventional myosin-IXb (Unconventional myosin-9b)	M0R0P8;M0R300;Q13459;Q13459-2
E9PAT2	UPF0606 protein KIAA1549L	E9PAT2;H0YDE5;Q6ZVL6;Q6ZVL6-2
Q6EMK4	Vasorin (Protein slit-like 2)	Q6EMK4
Q9UPU3	VPS10 domain-containing receptor SorCS3	Q9UPU3
Q9HC57	WAP four-disulfide core domain protein 1 (Prostate stromal protein ps20) (ps20 growth inhibitor)	Q9HC57
Q86Y38	Xylosyltransferase 1 (EC 2.4.2.26) (Peptide O-xylosyltransferase 1) (Xylosyltransferase I) (XT-I) (XylT-I)	Q86Y38
F8VRY0	Zinc finger protein 385A	F8VRY0;F8VSJ1;F8VWV6;F8VY43;Q96PM9-1;Q96PM9-2

Table 4 discloses proteins whose peptides were found to be regulated by at least 60% in the CSF of AD patients compared to non-AD CSF when compared in a proteomics study without calibrator. Significance is not considered here. Same 6 CSF samples as in all calibrator studies. Column 1 = annotated ID during data search. Middle column = protein name/s given to matched sequence.

5 Final column = All Uniprot IDs that match to the peptide sequence detected at time of invention.

The biomarker panel may comprise phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and at least one, optionally two or more biomarkers selected from Table 1 and/or Table 2 and/or Table 3 and/or Table 4 and/or Table 2 or fragments thereof.

The biomarkers disclosed herein may be upregulated in the CSF of AD patients versus control like dynactin subunit-1 or may be down-regulated in the CSF patients versus control like cofilin-1.

Accordingly, in one embodiment the biomarker panel comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof; and cofilin-1 or a fragment thereof (e.g. a fragment having SEQ ID NO: 38) and/or dynactin subunit 1 or a fragment thereof (e.g. a fragment having SEQ ID NO: 37).

Optionally, the biomarker panel may also comprise at least one, or at least two or more, optionally at least three or all biomarkers selected from the group of ubiquitin carboxy-terminal hydrolase L1,

vitamin D binding protein Peroxiredoxin-1, MARCKS-related protein, Moesin, Actin, Protein TMSB4XP4, ApoE, Gelsolin, Secretogranin, Albumin and complement proteins, Apolipoprotein E, Secretogranin-1, Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform, Cytoplasmic dynein 1 heavy chain 1, RuvB-like 1, cDNA FLJ54806, Alpha-1-acid glycoprotein 2, Ras-related protein Rab-13, Serum albumin and Pigment epithelium-derived factor or fragments thereof.

In another embodiment of the invention, the biomarker panel may comprise phospholuciferase 1 having or comprising SEQ ID NOs: 1, 6-13 and thymosin beta-4 having or comprising SEQ ID NOs: 2, 14-16 and optionally Vitamin D-binding protein having or comprising SEQ ID NOs: 5 and 18 and/or Ubiquitin carboxyl-terminal hydrolase isozyme L1 having or comprising SEQ ID NOs: 4 or 17, or fragments thereof, preferably the panel further comprises at least one or more of the following biomarkers, or fragments thereof, dynactin subunit 1 having or comprising SEQ ID NO: 37 or SEQ ID NO: 57, cofilin 1 having or comprising SEQ ID NO: 38 or SEQ ID NO: 58), Apolipoprotein E having or comprising SEQ ID NO: 19; SEQ ID NO: 39 or amino acids 19 to 317 of SEQ ID NO: 39, Secretogranin-1 having or comprising SEQ ID NO: 20; SEQ ID NO: 40; or amino acids 21 to 677, 440 to 513 or 617 to 673 of SEQ ID NO: 40, Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform having or comprising SEQ ID NO: 21 or SEQ ID NO: 41, Cytoplasmic dynein 1 heavy chain 1 having or comprising SEQ ID NO: 22; SEQ ID NO: 42 or amino acids 2 to 4646 of SEQ ID NO: 42, RuvB-like 1 having or comprising SEQ ID NO: 23 or SEQ ID NO: 43), cDNA FLJ54806 having or comprising SEQ ID NO: 24 or SEQ ID NO: 44, Alpha-1-acid glycoprotein 2 having or comprising SEQ ID NO: 25; SEQ ID NO: 45 or amino acids 19 to 201 of SEQ ID NO: 45, Ras-related protein Rab-13 having or comprising SEQ ID NO: 26 or SEQ ID NO: 46, Serum albumin having or comprising SEQ ID NO: 27; SEQ ID NO: 47 or amino acids 19 to 22 or 25 to 609 of SEQ ID NO: 47, Pigment epithelium-derived factor having or comprising SEQ ID NO: 28; SEQ ID NO: 48 or amino acids 20 to 418 of SEQ ID NO: 48), Serum amyloid A-4 protein having or comprising SEQ ID NO: 29; SEQ ID NO: 49 or amino acids 19 to 130 of SEQ ID NO: 49, apolipoprotein A-I and its truncated version having or comprising SEQ ID NO: 30; SEQ ID NO: 50 or amino acids 19 to 267, 1 to 242, 25 to 267 or 25 to 266 of SEQ ID NO: 50, Fibrinogen alpha chain having or comprising SEQ ID NO: 31; SEQ ID NO: 51 or amino acids 20 to 35 or 36 to 866 of SEQ ID NO: 51, Haptoglobin having or comprising SEQ ID NO: 32; SEQ ID NO: 52 or amino acids 19 to 406, 19 to 160 or 162 to 406 of SEQ ID NO: 52, Alpha-1-antitrypsin having or comprising SEQ ID NO: 33; SEQ ID NO: 53 or amino acids 25 to 418 or 375 to 418 of SEQ ID NO: 53), Ig mu chain C region (SEQ ID NO: 34 or SEQ ID NO: 54, Hemoglobin subunit delta having or comprising SEQ ID NO: 35 or SEQ ID NO: 55, IgG Fc-binding

protein having or comprising SEQ ID NO: 36; SEQ ID NO: 56 or amino acids 24 to 5405 of SEQ ID NO: 56, or MARCKS-related protein having or comprising SEQ ID NO: 59.

For a list of the sequences used herein, Table 5 below shows the sequence correlation list.

Table 5

Biomarker name	SEQ ID NO:
Phosphoglucomutase 1 (human) (Uniprot P36871)	1
Thymosin Beta-4 (human) (Uniprot P62328)	2
Isoform 2 of Phosphoglucomutase 1	3
Ubiquitin carboxy-terminal hydrolase L1 (D6R956)	4
Vitamin D binding protein (D6RBJ7)	5
Phosphoglucomutase 1 (human) – peptide 1	6
Phosphoglucomutase 1 (human) – peptide 2	7
Phosphoglucomutase 1 (human) – peptide 3	8
Phosphoglucomutase 1 (human) – peptide 4	9
Phosphoglucomutase 1 (human) – peptide 5	10
Phosphoglucomutase 1 (human) – peptide 6	11
Phosphoglucomutase 1 (human) – peptide 7	12
Phosphoglucomutase 1 (human) – peptide 8	13
Thymosin Beta-4 (human) – peptide 1	14
Thymosin Beta-4 (human) – peptide 2	15
Thymosin Beta-4 (human) – peptide 3	16
Ubiquitin carboxy-terminal hydrolase L1 - peptide 1	17
Vitamin D binding protein - peptide 1	18
Apolipoprotein E – peptide 1	19
Secretogranin 1 – peptide 1	20
Serine/threonine protein phosphate 2A 65KDa regulatory subunit A alpha isoform – peptide 1	21
Cytoplasmic dynein 1 heavy chain 1 – peptide 1	22
RuvB-like 1 – peptide 1	23
cDNA FLJ54806	24
Alpha-1-acid glycoprotein 2 – peptide 1	25
Ras-related protein Rab13 – peptide 1	26
Serum Albumin	27
Pigment epithelium-derived factor – peptide 1	28
Serum Amyloid A-4 protein – peptide 1	29
Truncated apolipoprotein A-I – peptide 1	30
Fibrinogen alpha chain – peptide 1	31
Haptoglobin – peptide 1	32
Alpha-1-antitrypsin – peptide 1	33
Ig mu chain C region – peptide 1	34
Hemoglobin subunit delta – peptide 1	35
IgG Fc-binding protein – peptide 1	36
Dynactin Subunit 1 – peptide 1	37
Cofilin-1 – peptide 1	38
Apolipoprotein E (P02649)	39
Secretogranin 1 (P05060)	40
Serine/threonine protein phosphate 2A 65KDa regulatory subunit A alpha isoform (P30153)	41
Cytoplasmic dynein 1 heavy chain 1 (Q14204)	42

RuvB-like 1 (Q9Y265, H7C4G5, E7ETR0, H7C4I3, J3QLR1, B5BUB1)	43
cDNA FLJ54806 (MGEA5), mRNA (B4DYV7)	44
Alpha-1-acid glycoprotein 2 (P19652)	45
Ras-related protein Rab13 (P51153)	46
Serum Albumin (P02768, Q16167, H0YA55, B7WNR0, D6RHD5, H7C013, Q56G89, D6RCE7, Q6LEH2)	47
Pigment epithelium-derived factor (P36955)	48
Serum Amyloid A-4 protein (P35542)	49
Truncated apolipoprotein A-I (P02647)	50
Fibrinogen alpha chain (P02671)	51
Haptoglobin (P00738, J3QLC9, H0Y300, H3BS21, J3QR68, J3KRH2, J3QQI8, H3BMJ7, J3KSV1, Q14552)	52
Alpha-1-antitrypsin (P01009, G3V2B9, G3V5R8, G3V544, G3V387, G3V4I7, Q13747, A7L8C5, A7L8C6)	53
Ig mu chain C region (P01871)	54
Hemoglobin subunit delta (P02042, E9PEW8, E9PFT6, C9JRG0)	55
IgGFC-binding protein (Q9Y6R7)	56
Dynactin Subunit 1 (Q14203)	57
Cofilin-1 (P23528)	58
MARCKS-related protein (P49006)	59

The biomarker panels described herein are useful for diagnosing, for staging and for assessing the likelihood of developing a neurocognitive disorder, in particular Alzheimer's disease. The use of the biomarker panels according to the present invention in any of such methods has considerable advantages. Firstly, these biomarker panels translate events and changes in pathways that occur in the brain into a peripheral signal, they allow replacing tissue testing with a peripheral fluid testing. This represents a great advantage especially as the tissue primarily affected in neurocognitive disorder is the brain tissue. Brain biopsies are not carried out and the only tissue analysis carried out is post-mortem. Secondly, these biomarker panels have been developed as capable to translate early events and changes in pathways in the brain, such as neuroinflammatory events, which are believed to be the hallway of neurocognitive disorders characterized by microglia activation, such as Alzheimer's disease. Thirdly, these biomarker panels encompass biomarkers which are not those typically reported in the literature or currently used in the clinical setting, thus lending to clinician additional tools for identifying and distinguish, at an early stage, subjects who have AD and subjects who, despite presenting symptoms of neurocognitive impairment are not affect by the early signs of AD.

Hence, the present invention provides for a method for diagnosing a neurocognitive disorder in a subject, the method comprising:

- a) assaying a sample obtained from said subject for the biomarkers of a biomarker panel;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether that subject has a neurocognitive disorder by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the biomarker panel comprises:

- i. phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
- ii. thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof.

The present invention also provides for a method for staging a neurocognitive disorder in a subject, the method comprising:

- a) assaying a sample obtained from said subject for the biomarkers of a biomarker panel;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining the stage of the neurocognitive disorder in said subject by comparing said concentration or amount of each of the biomarkers of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers, wherein the biomarker panel comprises:
 - i. phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
 - ii. thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof.

The present invention also provides for a method for assessing in a subject the likelihood of developing a neurocognitive disorder, the method comprising:

- a) assaying a sample obtained from said subject for the biomarkers of a biomarker panel;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether that subject is likely to develop a neurocognitive disorder by comparing said concentration or amount of each of the biomarkers of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers wherein the biomarker panel comprises:
 - i. phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
 - ii. thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof.

In some embodiments, the biomarker panel for use in the method for diagnosing, staging or assessing in a subject the likelihood of developing a the neurocognitive disorder comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof.

In some other embodiments, the biomarker panel for use in the method for diagnosing, staging or assessing in a subject the likelihood of developing a the neurocognitive disorder comprises phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof and, optionally ubiquitin carboxy-terminal hydrolase L1 which comprises or has an amino acid sequence of SEQ ID NO:4 or an isoform or a variant or a fragment thereof and/or vitamin D binding protein which comprises or has an amino acid sequence of SEQ ID NO: 5 or an isoform or variant or a fragment thereof.

In some embodiments of the methods described herein the neurocognitive disorder is selected from the group of mild cognitive impairment, Alzheimer's disease, vascular dementia, dementia with lewy bodies, fronto-temporal dementia or combinations thereof. Preferably, the neurocognitive disorder is Alzheimer's disease (AD).

In some of these embodiments of the method described herein, the neurocognitive disorder, preferably AD, is characterised by microglia activation.

In one embodiment of the present invention, the method for diagnosing a neurocognitive disorder in a subject comprises:

- a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether that subject has a neurocognitive disorder by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease and, optionally the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or

fragments thereof.

In another embodiment of the present invention, the method for staging a neurocognitive disorder in a subject comprises:

- a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining the stage of the neurocognitive disorder in said subject by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease and, optionally the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of the present invention, the method for assessing in a subject the likelihood of developing a neurocognitive disorder in a subject comprises:

- a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether that subject is likely to develop a neurocognitive disorder in said subject by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease and, optionally the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

The present invention also provides for a method for treating Alzheimer's disease in a subject, the method comprising:

- a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID

NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

5 c) determining whether that subject has Alzheimer's disease by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations or amounts of said biomarkers;

d) administering to said subject an Alzheimer's disease treatment selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof.

Optionally, the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

The present invention further provides for a method for aiding the prognosis of a treatment for Alzheimer's disease in a subject, the method comprising:

15 a) assaying a sample obtained from said subject for biomarkers of a biomarker panel;
b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether said treatment for Alzheimer's disease is successful by comparing said concentration or amount of each of the biomarker in said sample with reference concentrations or amounts of said biomarkers. Preferably the treatment for Alzheimer's disease is selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof. Optionally, the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

The sample used in the methods according to the present invention may be selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof.

In one embodiment, the sample is cerebrospinal fluid (CSF).

30 In one embodiment of the present invention, the method for diagnosing a neurocognitive disorder in a subject comprises:

a) assaying a sample obtained from said subject for biomarkers of a biomarker panel

comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

b) measuring in said sample the concentration or the amount of each of the biomarkers
5 of said biomarker panel;

c) determining whether that subject has a neurocognitive disorder by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease, wherein the sample is cerebrospinal fluid (CSF) and, optionally the
10 biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of the present invention, the method for staging a neurocognitive disorder in a subject comprises:

a) assaying a sample obtained from said subject for biomarkers of a biomarker panel
15 comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

b) measuring in said sample the concentration or the amount of each of the biomarkers
of said biomarker panel;

c) determining the stage of the neurocognitive disorder in said subject by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease, wherein the sample is cerebrospinal fluid (CSF) and, optionally the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected
25 from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of the present invention, the method for assessing in a subject the likelihood of developing a neurocognitive disorder in a subject comprises:

a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID
30 NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

b) measuring in said sample the concentration or the amount of each of the biomarkers
of said biomarker panel;

c) determining whether that subject is likely to develop a neurocognitive disorder in said

subject by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers; wherein the neurocognitive disorder is Alzheimer's disease, wherein the sample is cerebrospinal fluid (CSF) and, optionally, the biomarker panel further comprises at least one, alternatively two or more,
 5 biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment the method for treating Alzheimer's disease in a subject comprises:

- a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which
 10 comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
- b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether that subject has Alzheimer's disease by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations
 15 or amounts of said biomarkers;
- d) administering to said subject an Alzheimer's disease treatment selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof; wherein the sample is cerebrospinal fluid (CSF) and optionally, the biomarker panel further
 20 comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment the method for aiding the prognosis of a treatment for Alzheimer's disease in a subject comprises:

- a) assaying a sample obtained from said subject for biomarkers of a biomarker panel;
- 25 b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
- c) determining whether said treatment for Alzheimer's disease is successful by comparing said concentration or amount of each of the biomarker in said sample with reference concentrations or amounts of said biomarkers, and wherein the sample is cerebrospinal fluid (CSF). Preferably the
 30 treatment for Alzheimer's disease is selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof. Optionally, the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1,

2, 3, 4, 5, 6, 7, or 8 or fragments thereof. In the methods described herein, the subject is preferably a human subject, who may have or may have not been previously diagnosed with mild cognitive impairment.

In some embodiments, the human subject may be undergoing further clinical assessment of dementia.

In some embodiments of the methods described herein, the assaying in step a) and/or the measuring in step b) may further comprise:

- i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or
- 10 ii) detecting in said sample autoantibodies specific to each of said biomarkers; or
- iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or
- iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the
- 15 biomarker panel; or
- v) any combinations of i), ii), iii) and/or iv).

In particular, the assaying step a) and/or the measuring step b) may comprise detecting one or more fragments of said biomarker in the biomarker panel. Optionally, the sample is immobilised on a solid support.

20 Therefore, in one embodiment, the method for diagnosing Alzheimer's disease in a human subject comprises:

- a) assaying a cerebrospinal fluid (CSF) sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucosylase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or
 - 25 thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
 - b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;
 - c) determining whether that subject has Alzheimer's disease by comparing said
 - 30 concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers;
- wherein the assaying is step a) and/or the measuring in step b) may further comprise:

i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or

ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or

iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or

v) any combinations of i), ii), iii) and/or iv); and

optionally, the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of the present invention, the method for staging Alzheimer's disease in a human subject comprises:

a) assaying a cerebrospinal fluid (CSF) sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining the stage of Alzheimer's disease in said subject by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers;

wherein the assaying is step a) and/or the measuring in step b) may further comprise:

i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or

ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or

iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or

v) any combinations of i), ii), iii) and/or iv); and

optionally the biomarker panel further comprises at least one, alternatively two or more,

biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment of the present invention, the method for assessing in a subject the likelihood of developing Alzheimer's disease in a human subject comprises:

- a) assaying a cerebrospinal fluid (CSF) sample obtained from said subject for
 - 5 biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
 - b) measuring in said sample the concentration or the amount of each of the biomarkers
 - 10 of said biomarker panel;
 - c) determining whether that subject is likely to develop Alzheimer's disease by comparing said concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers;
- wherein the assaying is step a) and/or the measuring in step b) may further comprise:
 - 15 i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or
 - ii) detecting in said sample autoantibodies specific to each of said biomarkers; or
 - iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive
 - 20 mass labels; or
 - iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or
 - v) any combinations of i), ii), iii) and/or iv); and
- optionally the biomarker panel further comprises at least one, alternatively two or more,
 - 25 biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In another embodiment, the method for treating Alzheimer's disease in a human subject comprises:

- a) assaying a cerebrospinal fluid (CSF) sample obtained from said subject for
 - 30 biomarkers of the biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;
 - b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether that subject has Alzheimer's disease by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations or amounts of said biomarkers;

d) administering to said subject an Alzheimer's disease treatment selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof; wherein the assaying is step a) and/or the measuring in step b) may further comprise:

i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or

10 ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or

15 iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or

v) any combinations of i), ii), iii) and/or iv); and

optionally the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

20 In another embodiment the method for aiding the prognosis of a treatment for Alzheimer's disease in a human subject comprises:

a) assaying a sample obtained from said subject for biomarkers of a biomarker panel comprising phosphoglucosyltransferase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

25 b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether said treatment for Alzheimer's disease is successful by comparing said concentration or amount of each of the biomarker in said sample with reference concentrations or amounts of said biomarkers, wherein the treatment for Alzheimer's disease is selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof, and

wherein the assaying is step a) and/or the measuring in step b) may further comprise:

i) contacting said sample with one or more binding agents to each of said biomarkers of

the biomarker panel; or

ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive
5 mass labels; or

iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or

v) any combinations of i), ii), iii) and/or iv).

Optionally, the biomarker panel further comprises at least one, alternatively two or more,
10 biomarkers selected from any one of Tables 1, 2, 3, 4, 5, 6, 7, or 8 or fragments thereof.

In some preferred embodiments of all the methods described herein, the concentration or the amount of phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof is increased compared to its reference concentration or amount.

15 In some other preferred embodiments of all the methods described herein, the concentration or the amount of thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof is increased compared to its reference concentration or amount.

In some other preferred embodiments of all the methods described herein, the concentration or the amount of phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ
20 ID NO:1 or an isoform or a variant or a fragment thereof is increased compared to its reference concentration or amount and the concentration or the amount of thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof is increased compared to its reference concentration or amount.

The present invention further provide for a method for identifying biomarkers in a sample
25 obtained from a subject, wherein the biomarkers are suitable for diagnosing or staging Alzheimer's disease, wherein the method comprises using activate microglia cells (e.g. BV2 cells) and/or their culture media in mass spectrometry and/or wherein the biomarkers are identified in said sample by using activated microglia cells as a reference. Preferably the biomarker panel comprises the biomarkers as defined herein. The sample as described above may be selected
30 from the group of CSF, blood, serum or plasma.

2. Kits

The present invention also provides for kits comprising reagents for assaying and/or measuring in a sample biomarkers of a biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a
 5 variant or a fragment thereof.

Optionally, the biomarker panel further comprises at least one, alternatively two or more, biomarkers selected from any one of Tables 1, 2, 3, or 4 or fragments thereof.

Preferably, the kit allows the diagnosing and staging of neurocognitive disorders, in particular Alzheimer's disease.

10 The reagents of the kits according to the invention may comprise one or more binding agents which specifically bind to the biomarkers of the biomarker panels. Preferably, the one or more binding agents are primary antibodies, wherein each primary antibody specifically binds to a different biomarker of the biomarker panel.

More preferably, the primary antibodies are antibodies against human phosphoglucomutase 1
 15 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or human thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof.

The primary antibodies may be immobilised on an assay plate, beads, microspheres or particles. Optionally, beads, microspheres or particles may be dyed, tagged or labelled.

20 When the kits comprise primary antibodies against the biomarkers of the biomarker panel, the kits may further comprise one or more secondary antibodies which specifically bind to said primary antibodies.

Optionally, the secondary antibodies may be labelled for example fluorescent labelled or tagged.

The kits according to the invention may further comprise one or more detection reagents for
 25 detecting the presence of the tagged secondary antibodies.

The sample is selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof.

The kits of the invention allows the user to:

a) assay a sample obtained from a subject for the biomarkers of the biomarker panel comprising phosphoglucomutase 1 which comprises or has the amino acid sequence of SEQ ID NO:1 or an isoform or a variant or a fragment thereof; and/or thymosin beta-4 which comprises or has the amino acid sequence of SEQ ID NO:2 or a variant or a fragment thereof;

5 b) measure in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determine whether that subject has a neurocognitive disorder, in particular Alzheimer's disease, by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations or amounts of said biomarkers;

10 In particular, the kits according to the invention may instruct the user to assay (as in step a)) and/or to measure (as in step b)) the sample by:

i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or

ii) detecting in said sample autoantibodies specific to each of said biomarkers; or

15 iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or

iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or

20 v) any combinations of i), ii), iii) and/or iv).

In yet another embodiment, the kits may comprise reagents suitable for preparing brain tissue, optionally for preparing formalin-fixed paraffin-embedded brain tissue sections.

The kit may additionally provide a reference which provides a quantitative measure by which determination of a concentration or amount of one or more biomarkers can be compared. The
25 reference may indicate the amount or concentration of biomarkers which indicate the presence or staging or likelihood of developing a neurocognitive disorder in particular AD.

The kit may also comprise printed instructions for performing the methods according to the present invention.

In one embodiment, the kit may be for performance of a mass spectrometry assay and may
30 comprise a set of reference peptides (e.g. SRM peptides) in an assay compatible format wherein each peptide in the set is uniquely representative of each of the biomarkers provided in Tables 1, 2, 3, 4, 5, 6, 7, or 8. Preferably two or more of such unique peptides are used for each biomarker

for which the kit is designed, and wherein each set of unique peptides are provided in known amounts which reflect the amount or concentration of such biomarker in a sample of a healthy subject.

5 Optionally, the kit may also provide protocols and reagents for the isolation and extraction of the biomarkers according to the invention from a sample, a purified preparation of a proteolytic enzyme such as trypsin and a detailed protocol of the method including details of the precursor mass and specific transitions to be monitored. The peptides may be synthetic peptides and may comprise one or more heavy isotopes of carbon, nitrogen, oxygen and/or hydrogen.

10 Optionally, the kits of the present invention may also comprise appropriate cells, vessels, growth media and buffers.

3. Detection and measurement of biomarkers

The biomarker panels described herein comprise both biomarkers where expression is modulated, i.e. quantitatively increased or decreased, and biomarkers which are exclusively present or absent, i.e. qualitatively expressed, in normal versus disease states. The degree to which expression differs in normal versus disease states need only be large enough to be visualised via standard characterisation techniques.

Methods for the detection and quantification of biomarkers are well known in the art and any suitable method may be employed.

20 In one embodiment, the biomarker(s) in the biomarker panel may be detected using a binding agent, such as an antibody, specific to that biomarker, for example in an ELISA assay or Western blotting.

Methods relating to the production of antibodies capable of specifically recognising one or more epitopes of the individual biomarkers in the biomarker panels described herein are known in the art. Such antibodies may include, but are not limited to, polyclonal antibodies, monoclonal antibodies (mAbs), humanised or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above.

30 For the production of antibodies, various host animals may be immunised by injection with a protein, or a portion thereof. Such host animals may include, but are not limited to, rabbits, mice and rats. Various adjuvants may be used to increase the immunological response, depending on

the host species, including active substances such as lysolecithin, Pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvant such as BCG bacille Calmette-Fuerin) and *Corynebacterium parvum*.

5 Polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of animals immunised with an antigen, such as target proteins, or an antigenic functional derivative thereof. For the production of polyclonal antibodies, host animals such as those described above, may be immunised by injection with differentially expressed or pathway protein supplemented with adjuvants as also described above.

10 Monoclonal antibodies, which are homogeneous populations of antibodies to a particular antigen, may be obtained by any technique, which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique of Kohler and Milstein (1975, *Nature* 256:495-7; and US Patent No: 4,376,110), the human β -cell hybridoma technique (Kosbor, et al., 1983, *Immunology Today* 4:72; Cole, et al., 1983, *Proc. Natl. Acad. Sci. USA* 80:2026-30), and the EBV-hybridoma technique (Cole, et al., 1985, *Monoclonal*
15 *Antibodies and Cancer Therapy*, Alan R. Liss Inc., pp. 77-96). Such antibodies may be of any immunoglobulin class including IgG, IgM, IgE, IgA, IgD and any subclass thereof. The hybridoma producing the mAb of this invention may be cultivated in vitro or in vivo. Production of high titers of mAbs in vivo makes this the presently preferred method of production.

20 In addition, techniques developed for the production of 'chimeric antibodies' (Morrison, et al., 1984, *Proc. Natl. Acad. Sci.* 81:6851-5; Neuberger, et al., 1984, *Nature* 312:604-8; Takeda, et al., 1985, *Nature* 314:452-4) by splicing the genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb
25 and a human immunoglobulin constant region.

Alternatively, techniques described for the production of single chain antibodies (US Patent No: 4,946,778; Bird, 1988, *Science* 242: 423-6; Huston, et al., 1988, *Proc. Natl. Acad. Sci. USA* 85:5879-83; and Ward, et al., 1989, *Nature* 334:544-6) can be adapted to produce differentially expressed or pathway protein-single chain antibodies. Single chain antibodies are formed by
30 linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide.

Antibody fragments, which recognise specific epitopes, may be generated by known techniques.

For example, such fragments include, but are not limited to, the F(ab')₂ fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternative, Fab expression libraries may be constructed (Huse, et al., 1989, Science 246:1275-81) to allow rapid and easy
5 identification of monoclonal Fab fragments with the desired specificity.

In some embodiments of the methods described herein, the sample may be immobilised on a solid support for analysis. An antibody sandwich technique may be employed in which binding agents, such as antibodies, specific for the individual biomarkers in the biomarker panel are immobilized on a solid support such as a planar surface or a microparticle bead and biomarkers
10 in the panel are captured by the immobilised binding agents, such as immobilized antibodies. The captured biomarkers are then detected using a second binding agent, such as a secondary antibody, that may be directly labelled with a signal generating agent (enzyme, fluorescent tag, radiolabel etc.) or may be detected using further amplification (labelled secondary antibody, streptavidin/biotin systems with enzyme, fluorophore, radiolabel etc.). Other methods may
15 include, but are not limited to, one-dimensional or two-dimensional (2D) gel electrophoresis of samples. Such methods are followed by transfer to a solid surface using techniques such as Western blotting and subsequent detection using antibodies specific for the AD biomarkers.

In other embodiments, autoantibodies to the biomarkers may be detected using the Western blotting approach described above using samples from a healthy subject, a patient or
20 representative of AD, and then detecting the presence of auto-antibodies specific for the biomarker that are present in the sample, but not in healthy subjects.

An example of a non-antibody binding agent is an aptamer. Examples of aptamers include nucleic acid aptamers and peptide aptamers.

Alternatively, the biomarkers may be detected by, amongst others, silver staining of 2D gel
25 electrophoresis or mass spectrometry techniques including LS/MS/MS, MALDI-TOF, SELDI-TOF and TMT-SRM.

Other such standard characterisation techniques by which expression differences may be visualised are well known to those skilled in the art. These include successive chromatographic separations of fractions and comparisons of the peaks, capillary electrophoresis, separations
30 using micro-channel networks, including on a micro-chip, SELDI analysis and qPST analysis.

Chromatographic separations can be carried out by high performance liquid chromatography as

described in literature, the chromatogram being obtained in the form of a plot of absorbance of light at 280 nm against time of separation. The material giving incompletely resolved peaks is then re-chromatographed and so on.

5 Capillary electrophoresis is a technique described in many publications, for example in the literature "Total CE Solutions" supplied by Beckman with their P/ACE 5000 system. The technique depends on applying an electric potential across the sample contained in a small capillary tube. The tube has a charged surface, such as negatively charged silicate glass. Oppositely charged ions (in this instance, positive ions) are attracted to the surface and then migrate to the appropriate electrode of the same polarity as the surface (in this instance, the
10 cathode). In this electro-osmotic flow (EOF) of the sample, the positive ions move fastest, followed by uncharged material and negatively charged ions. Thus, proteins are separated essentially according to charge on them.

Micro-channel networks function similarly to capillaries and can be formed by photoablation of a polymeric material. In this technique, a UV laser is used to generate high energy light pulses that
15 are fired in bursts onto polymers having suitable UV absorption characteristics, for example polyethylene terephthalate or polycarbonate. The incident photons break chemical bonds with a confined space, leading to a rise in internal pressure, mini-explosions and ejection of the ablated material, leaving behind voids which form micro-channels. The micro-channel material achieves a separation based on EOF, as for capillary electrophoresis. It is adaptable to micro-chip form, each
20 chip having its own sample injector, separation column and electrochemical detector: see J.S.Rossier et al., 1999, Electrophoresis 20:727-31.

Surface enhanced laser desorption ionisation time of flight mass spectrometry (SELDI-TOF-MS) combined with ProteinChip technology can also provide a rapid and sensitive means of profiling biomarkers and is used as an alternative to 2D gel electrophoresis in a complementary fashion.
25 The ProteinChip system consists of aluminium chips to which protein samples can be selectively bound on the surface chemistry of the chip (e.g. anionic, cationic, hydrophobic, hydrophilic, etc.). Bound biomarkers are then co-crystallised with a molar excess of small energy-absorbing molecules. The chip is then analysed by short intense pulses of N2 320nm UV laser with protein separation and detection being by time of flight mass spectrometry. Spectral profiles of each
30 group within an experiment are compared and any peaks of interest can be further analysed using techniques as described below to establish the identity of the biomarkers.

Isotopic or isobaric Tandem Mass Tags® (TMT® Thermo Scientific, Rockford, USA) technology

may also be used to detect biomarkers such as proteins of a biomarker panel described herein. Briefly, the proteins in the samples for comparison are optionally digested, labelled with a stable isotope tag and quantified by mass spectrometry. In this way, expression of equivalent proteins in the different samples can be compared directly by comparing the intensities of their respective isotopic peaks or of reporter ions released from the TMT® reagents during fragmentation in a tandem mass spectrometry experiment.

Detection of biomarkers of biomarker panels described herein may be preceded by a depletion step to remove the most abundant proteins from the sample. The large majority of the protein composition of serum/plasma consists of just a few proteins. For example, albumin, which is present at a concentration of 35-50 mg/ml, represents approximately 54% of the total protein content with IgG adding other 16%. In contrast, proteins changing in response to disease, for example as a result of tissue leakage, may circulate at 10ng/ml. This vast dynamic range of protein concentrations represents a major analytical challenge and to overcome the problem, a multiple affinity depletion column may be used to remove the most highly abundant proteins (e.g. the 2, 3, 4, 5, 6, 7, 8, 9 or 10 or more highly abundant proteins). This enables the detection of changes in lower abundance ranges because more starting material can be used and there is less interference from the highly abundant molecules. Such a depletion strategy can be applied before any detection method.

4. Method to screen and select test agents for the treatment of neurocognitive disorders

The biomarker panels described herein may be used to test agents for the ability to prevent or ameliorate neurocognitive disorders, such as AD, or one or more symptoms thereof.

Such agents may be tested in human subjects in clinical trials. Any agent which restores the expression of the proteins in a biomarker panel described herein towards levels found in healthy individuals or towards its absence or presence as the case may be, is of potential use in treating a neurocognitive disorder, such as AD, i.e. reducing AD symptoms or slowing the progression of AD.

During clinical trials, for example, the amount or concentration of one or more biomarkers of a biomarker panel as described herein can be determined in the presence or absence of the agent being tested. The efficacy of the agent can be followed by comparing the expression data obtained to the corresponding known expression patterns in a normal state. Agents exhibiting efficacy are those which alter the presence, amount or concentration of the biomarkers in the biomarker panel to more closely resemble that of the normal state.

The detection of the biomarkers in the biomarker panel in the neurocognitive disorder relative to their expression or presence in a normal state can also be used for monitoring the efficacy of potential agents for the treatment of a neurocognitive disorder, such as AD, during clinical trials. During clinical trials, the level and/or presence of the biomarkers in the biomarker panel can be
5 determined in cerebrospinal fluid (CSF) in the presence or absence of the agent being tested. The efficacy of the agent can be followed by comparing the biomarker levels and/or presence of the biomarkers in the data obtained, to the corresponding known levels/presence for the cells and/or tissues and/or body fluids in a normal state. Agents exhibiting efficacy are those which alter the presence, amount or concentration of the biomarker panel of the cell and/or tissue
10 sample and/or body fluid from a subject to more closely resemble that of the normal state or which stabilise the pattern i.e. prevent progression of the disease. Because the present biomarker panels translate events and changes in pathways that occur in the brain into a peripheral signal, they allow replacing tissue testing with a peripheral fluid testing. This represents a great advantage especially as the tissue primarily affected in neurocognitive
15 disorder is the brain tissue. Brain biopsies are not carried out and the only tissue analysis carried out is post-mortem.

With regard to intervention, any treatments that restore or partially restore the expression of biomarkers in a biomarker panel described herein to healthy levels should be considered as candidates for therapeutic intervention in neurocognitive disorders such as AD. Dosages of test
20 agents may be determined by deriving dose-response curves.

Similarly, any treatments that can prevent the development of neurocognitive disorders such as AD or prevent progression to levels of more advanced AD should be considered as candidates for the AD therapeutic intervention.

An agent may be selected if it prevents or slows the change over time in presence, concentration
25 or amount of the biomarkers of the biomarker panels relative to controls.

Preferably, the agent is selected if it converts the amount or concentration of a biomarker of the biomarker panels towards that of a normal subject.

The agent may be selected if it slows or stops the change of concentration or amount over time. For example, agents which exhibit inhibitory activity, may be used in accordance with the
30 invention to prevent mild cognitive impairment or AD symptoms. Such molecules may include, but are not limited to, peptides (such as, for example, peptides representing soluble extracellular portions of target protein transmembrane receptors), phosphopeptides, small organic or inorganic

molecules, or antibodies (including, for example, polyclonal, monoclonal, humanised, anti-idiotypic, chimeric or single chain antibodies, and Fab, F(ab')₂ and Fab expression library fragments, and epitope-binding fragments thereof).

5. Examples

5 Certain aspects and embodiments of the invention will now be illustrated by way of example and with reference to the figures and tables described above. All documents mentioned in this specification are incorporated herein by reference in their entirety for all purposes.

All reagents for the cell culture and samples preparation were purchased from Sigma Aldrich® (Dorset, UK) unless stated. Tandem Mass Tags® (Thermo Scientific®); Acetonitrile (Fisher
10 Scientific®, Loughborough, UK); Trypsin (Roche Diagnostics®, West Sussex, UK).

BV2 cells samples – BV2 cells were seeded into 6 well plates at 80,000 cells per well and maintained at 37°C at 5% CO₂. Cells were cultured for 24 hours in Dulbecco's modified eagle medium (Gibco®, Life Technologies) with 10% fetal bovine serum (Gibco®) supplemented with 2mM L-glutamine, 100U/mL penicillin and 100mg/mL streptomycin, gentamycin and mycoplasma
15 removal agent (AbD Serotec®). To activate the cells, a solution made of 2µg/ml lipopolysaccharide (LPS) and 10ng/ml interferon-gamma (IFNγ) (R&D Systems®)(Gordon S, et al., Nat Rev Immunol. 2005, 5, 12, 953-64. Dale DC, et al., Blood. 2008, 15, 112, 4, 935-45) was applied for 24 hours prior to harvesting. Cells were lysed in 8M urea, 75mM NaCl, 50mM Tris (pH 8.2) before sonication on ice (20 x 1sec 20% amplitude) and centrifuged at 12,500g for 10mins at
20 4°C. The protein concentration of the cell lysate was estimated by Bradford assay. Samples were aliquoted to prevent freeze-thawing and stored at -80°C. The BV2 cells samples will be referred herein after as "calibrator" as they will be used to create calibration curves in the following experiments.

Cerebrospinal fluid samples – CSF samples were from subjects who sought medical advice
25 because of cognitive impairment. Subjects were designated as normal or AD according to CSF biomarker concentrations using cutoffs that are 90% sensitive and specific for AD): total tau (T-tau) >350 ng/L, phospho-tau (P-tau) >80 ng/L and Aβ₄₂ <530 ng/L (Hansson O, et al., Lancet Neurol. 2006, 5:228-34. None of the biochemically normal subjects fulfilled these criteria. CSF T-tau, P-tau and Aβ₄₂ concentration were determined using INNOTEST enzyme-linked
30 immunosorbent assays (Fujirebio, Ghent, Belgium) by board-certified laboratory technicians according to protocols approved by the Swedish Board for Accreditation and Conformity Assessment (SWEDAC). The study was approved by the regional ethics committee at the

University of Gothenburg.

In-Solution Tryptic Digest and Tandem Mass Tag® (TMT®)labelling – Following solubilization and denaturation in 100mM TEAB buffer and 0.1% sodium dodecyl sulphate (SDS), the CSF samples and the BV2 cell-line (calibrator) were reduced with 1mM TCEP at 55 °C for 60 min and alkylated
5 with 7.5mM iodoacetamide at room temperature for 60 min. Trypsin was used for digestion at an approximate 1:25 weight ratio of trypsin-to-total protein and incubated at 37 °C overnight (~18 h). Following digestion, the peptides obtained were labeled with one of the TMT® 10-plex reagents at 15mM and incubated for 60 min at room temperature. To quench the TMT® reaction, 0.25% hydroxylamine was added to each sample and incubated for 15 min. The samples were then
10 combined to generate an analytical sample comprising a 1:10 calibration curve of non-activated BV2 cells, a 1:10 calibration curve of activated BV2 cells and equal amount of six CSF samples and incubated for a further 15 min (Figure 6). Each sample was desalted using RP18 columns (Waters, Manchester, UK) and excess reagents and SDS were removed by strong cation exchange (SCX) purification. Peptides were eluted in 75% acetonitrile (ACN) + 400mM NH₄Oac
15 (Ammonium Acetate) and dried to completion. For mass spectrometry (MS) analysis the sample was resuspended in 2% ACN + 0.1% formic acid.

LC-MS/MS - Quantitative analysis was performed in triplicate using an Orbitrap Fusion Tribrid® mass spectrometer (Thermo Scientific®) in the positive mode with EASYnLC1000 system and a 50cm EASY-Spray column (Thermo Scientific®). The column temperature was maintained at
20 40°C, and the peptides were separated at a flow rate of 200 nL/min.

Peptides were eluted from the column over a 300 min gradient, from 3% to 30% solvent B (acetonitrile with 0.1% formic acid) in 280 min, followed by an increase to 80% solvent B in 10mins, which was held for a further 10mins. Solvent A was water with 0.1% formic acid. Wash and blank LC–MS/MS runs preceded the analysis.

25 A Top10 CID-HCD MS3 SPS method with a 2 second cycle time was utilized and the parameters were as follows: MS; Spray voltage - 2000V; ion transfer tube temperature - 275 °C; detector – Orbitrap; scan range (m/z) - 400-1400; resolution – 120000; AGC target - 5x10⁵. MS/MS (CID); Isolation mode – quadrupole; collision energy – 35%; detector – Ion trap; AGC target - 4x10³. MS3 (HCD); detector – Orbitrap; collision energy – 55%; scan range – 100-1000 m/z; resolution
30 power – 30000; AGC target - 6x10⁴.

Bioinformatics - LC-MS/MS data was initially processed using SequestHT and Mascot within Proteome Discoverer 1.4, against the Uniprot human protein database

(ftp://ftp.uniprot.org/pub/databases/uniprot/current_release/knowledgebase/peptomes/). After applying a 5% false discovery rate (FDR)) to filter the data in Proteome Discoverer, the number of peptide and protein identifications was determined.

Experiment A

- 5 This experiment was designed to incorporate two 2-point calibration curves using the control (i.e. non-activated) BV2 cells and activated (IFN- γ + LPS) BV2 cells, alongside six (6) CSF samples constituted of three (3) AD CSF samples and 3 non-AD CSF samples); 3 AD CSF samples were compared with three (3) non-AD control CSF samples using a two x 2-point calibration curve of control and activated BV2 cells to detect biomarkers of activation in a 3 vs 3 vs 2 vs 2 TMT®
- 10 10-plex MS3 method. The experiment was designed so that the protein content from the BV2 cells dominated the total protein content in the sample. The two x 2-point calibration curve samples were spiked at a ratio of 1:10 and the 6 CSF samples were calculated to fall within this range. The total protein content that can be injected onto the MS column is 2 μ g, therefore, the CSF samples' protein content per inject is limited to 121ng per channel per CSF sample.
- 15 All CSF samples and the BV2 cells samples were solubilised, reduced and alkylated (as outlined above) prior to overnight tryptic digestion. Subsequently, all peptide samples were TMT® labelled as below, using the TMT¹⁰plex reagents:
- 126 – control CSF 1
 - 127e – control CSF 2

20 • 127 – control CSF 3

 - 128e – AD CSF 1
 - 128 – AD CSF 2
 - 129e – AD CSF 3
 - 129 – non-activated BV2 cell line

25 • 130e – non-activated cultured BV2 cell line

 - 130 – IFN γ + LPS activated BV2 cell line
 - 131 – IFN γ + LPS activated BV2 cell line

The TMT¹⁰plex labelled samples were mixed so as to generate a 1:10 calibration curve for the resting cells (channels 129 & 130e), a 1:10 calibration curve for the activated cells (channels 130

30 & 131) and equal levels of the 6 CSF samples wherein the total protein content from the cell digests is approximately double that for the CSF samples (Figure 6). The mixed analytical sample was de-salted and cleaned (excess TMT® labels removed) and split into 2. Half of the sample

was frozen and the remainder was fractionated by high pH reverse phase fractionation into 8 separate fractions. These were analysed on the new generation Orbitrap Fusion using a gradient of 3 hours.

5 The raw data files from all MS injections were searched using SequestHT and Mascot in Proteome Discoverer 1.4, against the Uniprot human protein database.

The reporter ion signal intensities from the 6 CSF channels were normalised by sum-scale normalization, a mathematical approach to remove experimental bias. The process involves summing the intensity values for all analytes measured in a given sample and then calculating the median value across all the summed values. The median value is divided by each summed value
10 to create a correction factor which is multiplied to the original intensity values to give the normalized sum scaled measurement (Robinson MD, et al., Bioinformatics 2010, 26:139–40; De Livera AM, et al., Anal. Chem. 2012, 84, 24, 10768–76) and the variability across the CSF dataset was investigated using Principle Component Analysis (PCA) plots. It was found that the CSF samples separate by disease status at the peptide and protein level with the first principle
15 component accounting for 79.9% of the total variation leading to group separation (data not shown).

In the first analysis of the MS data, the ratio of the signal intensity in the calibrator channels (129, 130e, 130 and 131) was expected to be 1:10 for the non-activated (129 and 130e) and 1:10 in the activated cells (130 and 131). The observed intensities across the two non-activated cell
20 channels and across the two activated cell channels (calibrator) was calculated for every single peptide. Peptides with a ratio of $1:10 \pm 15\%$ were considered to be acceptable calibrators. Only 22 peptides were found to contain an acceptable calibrator using these parameters.

In a second approach to identify which peptides show regulation with disease, the log2 ratio of the average signal intensities in the three AD CSF samples compared to the average signal in the
25 three control CSF samples was determined. A p-value for this ratio was established following a 2-sample t-test across the two CSF groups for every single peptide and protein (providing a signal was present in all 6 of the CSF TMT® channels). The log2 ratio of the two calibrator channels in the non-activated cells and the activated cells was also calculated to show which peptides are regulated with BV2 cell activation. The ratio was calculated for the low spike
30 calibrator in activated and control cells, and also for the high spike calibrator.

A total of 564 peptides were found to be up-regulated by at least 60% in the activated vs control BV2 cells (filtered for 60% increase in both the high and low calibrator ratio's). These were shown

to map to 9 KEGG pathways, the most significant being the complement and coagulation cascades pathway, followed by the glycolysis/glycogenesis, the prion disease, the amino and nucleotide sugar metabolism, the antigen processing and presentation, the extracellular matrix-receptor interaction, the focal adhesion, the regulation of actin cytoskeleton and alanine/aspartate/glutamate metabolism pathways.

This first data set processing included all the peptides detected, regardless of missing TMR® reporter ion channels and allow the identification of peptides that are present in the CSF of AD patients that are absent in controls, or similarly, peptides which are present in activated BV2 cells that are not present in non-activated BV2 cells.

- 10 Of the 564 peptides up-regulated in activated BV2 cells, 75 were also found to be at least 60% elevated in AD CSF compared to control CSF. These 75 peptides map to 58 proteins as listed in Table 1. Proteins which are well known to be elevated in the brain of AD patients like Peroxiredoxin (Kim SH et al., J Neural Transm Suppl. 2001;(61):223-35)(Figure 3A) and are considered biomarkers of oxidative stress (Poynton RA et al., Biochim Biophys Acta. 2014, 15 1840:906-12) are present along with proteins well known to be elevated in BV2 cells upon activation by LPS for example MARCKS-related protein (Figure 3B), (Sunohara JR et al., J Neurochem. 2001 78:664-72) and amyloid-beta (Murphy A et al., Neurosci Lett. 2003, 347:9-12); Moesin (Figure 3C), part of the extra-cellular matrix complex, which helps in the non-amyloidogenic processing of APP; Actin (Figure 3D), known to be increased in AD patients' CSF, specifically in those individuals carrying the ApoE4 allele (Merched A et al., FEBS Lett. 1998, 20 425:225-8.).

From the list of regulated peptides, 35 peptides from 29 proteins had a signal in all 10 channels, with 4 peptides having significant regulation ($p \leq 0.05$) as shown in Table 6.

Table 6

SEQ ID NO:	Peptide	Protein	P value
6	QFSANDK	Phosphoglucomutase-1	0.031
14	NPLPSKETIEQEK	Thymosin beta-4	0.050
17	QIEELKGQEVSPK	Ubiquitin carboxyl-terminal hydrolase isozyme L1	0.047
18	HQPQEFPTYVEPTNDEICEAFRK	Vitamin D-binding protein	0.002

These peptides are found to be regulated by at least 60% with BV2 cell activation and are significantly up-regulated by at least 60% in the CSF of AD patients (Figure 4A-D). Peptide NPLPSKETIEQEK (SEQ ID NO: 14) is found in both TMSB4XP4 protein and homologous protein Thymosin beta-4. The protein sequences of these two proteins are identical apart from the first 19 residues of TMSB4XP4 which are absent in Thymosin beta-4.

Phosphoglucomutase 1 was not detected when the CSF samples were measured in the absence of the BV2 cell sample calibrator, whilst Thymosin beta-4 was detected in both settings. Of the total eight (8) peptides detected for Phosphoglucomutase 1 (Table 7), 5 were regulated ($\geq 60\%$; in bold in Table 7) but not significantly and only one was found to be significantly regulated with a P value ≤ 0.05 (QFSANDK; SEQ ID NO:6).

Three (3) peptides were detected for Thymosin beta-4 but only peptide NPLPSKETIEQEK (SEQ ID NO:14) was significantly regulated (Table 7) with one other also regulated $\geq 60\%$ but not significantly (also in bold in Table 7).

Table 7

Phosphoglucomutase-1								
Peptide SEQ ID NO:	Control CSF	AD CSF	Calibrator				Log2_ AD/C	Pvalue (peptide)
QFSANDK 6	783.61	3435.34	6060	78200	17800	137000	1.799	0.0313
	1291.05	4495.23						
	2946.03	5220.72						
IDAMHGVV GPYVK 7	1167.54	4756.93	26300	40600 0	84500	654000	1.390	0.3109
	NA	5036.78						
	2673.66	20413.03						
VDLGVLGK 8	1194.79	2424.98	15600	20500 0	44600	376000	0.566	0.3430
	2901.17	4295.25						
	4574.59	15990.21						
LYIDSYEK 9	1200.04	855.75	693	13700	3100	24300	1.119	0.5194
	1406.51	3055.20						
	3993.841	6859.42						
SMPTSGAL DR 10	2822.50	2375.48	1930	29400	6470	42800	0.537	0.8801
	1003.93	464.43						
	1326.44	1925.31						
YDYEEVEA EGANK 11	442.82	NA	8410	14100 0	14400	119000	1.566	NA
	NA	649.20						
	NA	1973.66						
IALYETPTG	NA	623.68	8250	11500	26300	201000	-0.248	NA

WK 12	NA 938.10	789.49 6944.43		0				
QSVEDILK 13	NA 587.03 576.36	NA NA 3463.72	2900	41700	9360	59200	2.573	NA
Thymosin beta-4								
Peptide SEQ ID NO:	Control CSF	AD CSF	Calibrator				Log2_ AD/C	Pvalue (peptide)
NPLPSKETI EQEK 14	4033.76 7534.52 7128.95	11913.75 10537.66 18341.59	3810	56000	9160	122000	0.7409	0.0497
TETQKNPL PSK 15	3098.65 5362.34 5895.98	9727.02 6806.84 14528.34	8350	15500 0	23700	360000	0.8591	0.0819
ETIEQEK 16	19629.59 33720.30 39302.79	35338.74 37756.83 96515.70	2890	43300	7980	44200	0.1631	0.2858

When the data are filtered to identify peptides regulated in the CSF from AD samples compared to the non-AD samples, 1924 peptides were found to be up-regulated by at least 60% in AD CSF compared to non-AD CSF. A total of 63 peptides, mapping to 53 proteins were found to be significantly up-regulated ($p \leq 0.05$) as shown in Table 2. The list in Table 2 shows some proteins that are known to be regulated in AD CSF, like ApoE, Gelsolin, Secretogranin, Albumin and complement proteins. These examples demonstrate that the approach used herein allows the identification and quantification of peptides from well-known AD biomarkers which commonly appear in CSF in addition to peptides that represent novel CSF biomarkers of early changes in AD following microglia activation.

The top 10 most up-regulated peptides in AD CSF compared to non-AD and their corresponding proteins are shown in Table 8.

Table 8

Peptide SEQ ID NO:	Protein names	Log2_AD/C	Pvalue
AYKSELEEQLTPVAEETR 19	Apolipoprotein E	4.300	0.0024

GYPGVQAPEDLEWER 20	Secretogranin-1	3.717	0.0411
AVGPEITK 21	Serine/threonine-protein phosphatase 2A 65 kDa reregulatory subunit A alpha isoform	2.768	0.0121
LRDQLGTAK 22	Cytoplasmic dynein 1 heavy chain 1	2.759	0.0001
KTEITDK 23	RuvB-like 1	2.153	0.0445
WELNTYLYAPK 24	cDNA FLJ54806	2.115	0.0478
SDVMYTDWKK 25	Alpha-1-acid glycoprotein 2	2.050	0.0283
FFETSAK 26	Ras-related protein Rab-13	1.966	0.0467
DAHKSEVAHR 27	Serum albumin	1.901	0.0093
LKLSYEGETVK 28	Pigment epithelium-derived factor	1.887	0.0085

Down regulation was also observed, although the peptide numbers were much lower. Eight (8) peptides were down-regulated by at least 60% in the activated BV2 cells and in AD CSF, and only 1 of these, Serum amyloid A4 protein, had a significant p value ($p=0.014$) based on the 3 vs 3 CSF channels.

5

Table 9

Peptide SEQ ID NO:	Protein names	Log2_AD/C	Pvalue
EALQGVGDMGR 29	Serum amyloid A-4 protein	-1.067	0.0138
LAELYHAK 30	Truncated apolipoprotein A-I	-1.236	0.0194
TVIGPDGHK 31	Fibrinogen alpha chain	-1.389	0.1340
DIAPTLTLYVGK 32	Haptoglobin	-1.616	0.1480
SASLHLPK 33	Alpha-1-antitrypsin	-0.845	0.1816

FTCTVTHTDLPSPK 34	Ig mu chain C region	-2.516	0.3394
VLGAFSDGLAHLNLK 35	Hemoglobin subunit delta	-2.468	0.4325
ISVAQGASK 36	IgGFC-binding protein	-0.759	0.5297

Experiment B

In order to enhance the MS data acquisition from the BV2 cell line calibrator, experiment B was designed as a 4-point calibration curve to be spiked into the total combined CSF samples at a ratio of 1:4:6:10 in order to ensure the calibrator proteins dominated the overall protein content of the TMT® 10-plex sample. These are arbitrary values allowing to determine a suitable protein load from the CSF samples for analysis. Six individual CSF samples were combined at a 2:2:2:2:2:2 ratio, falling within the 4-point calibration curve.

As the maximum load on column is 2µg, the true protein load per channel can be determined by dividing the maximum 2µg by the total number of arbitrary values (x) needed, which in this case is 33 (4 calibrator channels plus 6 CSF channels). If 33x equals 2µg, 1x is therefore 0.06µg and this can then be used to determine the total amount of protein from each of the 10 channels contributing to the calibrator analytical sample. Just 0.12µg of each CSF sample is required (2x), along with a 4-point calibrator comprised of 0.06µg (1x), 0.24µg (4x), 0.36µg (6x) and 0.6µg (10x). This results in a total of 0.72µg of protein from all the CSF samples and 1.26µg of protein from the BV2 cell line calibrator – the calibrator proteins are therefore 1.75 fold more prevalent than the total CSF protein load.

The calibrator sample was analysed in triplicate on the Oribtrap Fusion Tribrid using an MS3 SPS method over a 300 minute gradient. The raw data files from all three MS injections were searched using SequestHT and Mascot in Proteome Discoverer 1.4, against the Uniprot human protein database. Results for the triplicate injections were merged resulting in one large data set for analysis. After applying a 5% false discovery rate (FDR) to filter the data in Proteome Discoverer, the number of peptide and protein IDs from calibrator-derived only, CSF sample derived only, and peptides common to both the microglia cell line calibrator and CSF samples, was determined. The design of this experiment ensured that the MS acquisition was driven by the more prevalent microglia cell line peptides, and this was evident in the peptide IDs recorded. No peptides specific to CSF samples were detected, confirming the premise that the calibrator approach circumvents the issues surrounding highly dominant CSF proteins. Instead, the peptides identified were either

specific to the BV2 microglia cells (2,317), or common to CSF and BV2 microglial cells (11,150). These shared peptides were the focus for further analysis to isolate any biomarkers of microglial cells activation present in the CSF. All peptides with signal for all 10 TMT® reporter ions were taken forward for processing through a set of in-house bioinformatics scripts developed in R.

- 5 The reporter ion signal intensities from the six CSF channels were normalized by sum-scale normalization. Following normalization the variability across the CSF dataset was investigated using Principal Component Analysis (PCA). Group separation of AD and control CSF was seen at the peptide and protein level, forming the first principal component, and accounting for 44.6% of the total variation seen in the dataset. The second principal component explained 19.6% of the variability in the dataset, and this corresponded to the biological variation within the groups.

To further filter the data, we normalized the cell line calibrator data to one of the calibrator channels (channel 129 as in the previous experiment). This was carried out for the four channels dedicated to calibrator, which allowed us to filter for an expected TMT® calibrator signal signature or pattern. Following normalization, the ratio of the signal intensity in channels 129, 130e, 130 and 131 (calibrator channels) was expected to be 1:4:6:10. To measure a correspondence between expected calibrator signal intensities to observed calibrator intensities, an R^2 value across all four channels was calculated for every single peptide. PSM level intensities for the four TMT® calibrator channels show marginal deviation from expected linear calibrator signal intensity ratio of 1:4:6:10. A 39.3% of the peptides had a calibrator R^2 of ≥ 0.95 and were taken on for further data analysis.

The normalized dataset, filtered for the presence of an expected linear calibrator signal intensity was further filtered based on the significance following a 2-sample t-test across the two CSF groups for every single peptide and protein. Peptides with a p value ≤ 0.05 were considered significant. The log2 ratio of the average AD CSF signal intensities (channels 128e, 128 and 129e) to control CSF signal intensities (channels 126, 127e and 127) was also normalized to the 129 TMT® calibrator channel. This provided a means of identifying which of the peptide sequences common to the activated microglia cell line and CSF samples were differentially regulated between control and AD CSF. We identified 84 unique peptide sequences from 77 proteins that were significantly up-regulated at least 60% ($\log_2$ ratio ≤ -0.7) in AD CSF compared to controls, and 34 unique peptides from 26 proteins that were significantly down-regulated by at least 60% ($\log_2$ ratio ≥ 0.7).

When the list of regulated peptides in the CSF of AD patients is analysed, the benefit of TMT®

calibrator over the traditional proteomics approach can be seen. As stated, the maximum protein load on the 75µm diameter analytical LC column per injection is 2µg. In the TMT® calibrator design the 2µg is split unequally between the 4-point calibrator and the six CSF samples (1:4:6:10 ratio for the calibrator, 2:2:2 for AD CSF and 2:2:2 for non-AD CSF). Without the addition of the calibrator, the six CSF samples could be labelled with TMT in a multiplex experiment, with 0.33µg combined from each sample per inject. This would not overcome the problems associated with high abundant CSF proteins which would dominate the MS acquisition, preventing lower abundant biomarkers from being detected. To highlight the different results seen after inclusion of the cell line calibrator, the same six CSF samples used in the TMT® calibrator study were equally combined and a total load of 2 µg was analysed in triplicate using the same method. Following the same bioinformatics processing, the results were filtered and analyzed to identify significantly regulated peptides in the AD CSF compared to control CSF samples. Seventy three proteins were significantly regulated by at least 60% (up or down regulation) in CSF but only 16 of these overlapped with significantly regulated peptides in the TMT® calibrator study. The majority of the proteins identified in the CSF samples are known to be secreted proteins, annotated as such under their Uniprot accession entries (such as plasminogen, mimecan and hemopexin). Intracellular biomarkers, such as proteins found commonly in the nucleus, are of particular interest. With the aid of the calibrator, it was possible to identify from the significantly regulated list total of 29 biomarkers which are localized in the nucleus. In the absence of the calibrator, only 5 proteins were found. A large proportion of the significantly regulated proteins found without TMT® calibrator are proteins that are commonly observed in CSF studies including serum albumin, complement proteins (C3, C5 and C7), fibrinogen gamma chain and Ig gamma chain (Boche D, et al., Neuropathol Appl Neurobiol. 2013, 39, 1, 3-18). These proteins are likely representative of disease related changes of low specificity rather than the cellular changes specific to AD. They are some of the most abundant proteins found in the CSF and are reported in the majority of CSF proteomic analysis studies (Hühmer AF, et al., Disease Markers. 2006, 22, 1-2, 3-26). In comparison, the majority of peptides derived when the BV2 cell line is used to drive the experiment are cellular and may represent a cellular response specific to disease. These include peptides from dynactin (Figure 5A), cofilin (Figure 5A), alcohol dehydrogenase, filamin-A, myosin proteins and Ras-related proteins. These are cellular proteins regulated in AD that would not have been detected if the CSF samples had been analysed in the absence of the BV2 cell samples (calibrator samples). Peptide IKDALVR (SEQ ID NO: 37), corresponding to dynactin subunit 1 (Figure 5A), was the most upregulated peptide whilst peptide MIYASSK (SEQ ID NO: 38), corresponding to Cofilin-1 (Figure 5B), was the most down regulated peptide in the CSF of AD patients when compared to non-AD controls.

To conclude, biomarkers are indicators of pathological processes and biological events. Their levels change as a result of disease and also in response to pharmacological intervention. The challenge is how to find these molecules in biofluids such as blood or CSF which contain a high protein dynamic range and hyper-abundant proteins such as albumin.

- 5 The inventors have applied a novel Tandem Mass Tag® (TMT®) mass spectrometry (MS) approach, the TMT® calibrator analysis, to look for biomarkers of microglia activation within the CSF of AD patients. BV2 cells are a microglial cell line derived from raf/myc-immortalised murine neonatal microglia (Blasi E, et al., J neuroimmunology. 1990, 27, 2-3, 229-37) and have been used extensively to study microglial activation. Studies have shown their utility as a surrogate for
- 10 primary microglial cultures which are costly in terms of animals used and time consuming to prepare (Henn A, et al., Alternatives to animal experimentation. 2009, 26, 2, 83-94; Stansley B, et al., J Neuroinflammation. 2012, 31, 9, 115).

The successful application of the TMT® calibrator analysis in this study has provided a novel list of potential biomarker candidates likely originating from activated microglia and circulating in CSF

15 and which are differentially expressed in AD patients compared with non-AD subjects.

Claims:

1. A biomarker panel comprising markers:
 - i) phosphoglucomutase 1 comprising or having the amino acid sequence of SEQ ID NO:1
 5 or an isoform or a variant or a fragment thereof;
 and/or
 - ii) thymosin beta-4 comprising or having the amino acid sequence of SEQ ID NO:2 or a
 variant or a fragment thereof.
- 10 2. The biomarker panel according to claim 1, wherein the panel further comprises ubiquitin
 carboxy-terminal hydrolase L1 which comprises or has an amino acid sequence of SEQ ID NO:4
 or an isoform or a variant or a fragment thereof.
- 15 3. The biomarker panel according to any one of claim 1 or claim 2, wherein the panel further
 comprises vitamin D binding protein which comprises or has an amino acid sequence of SEQ ID
 NO: 5 or an isoform or variant or a fragment thereof.
- 20 4. The biomarker panel according to any one of claims 1 to 3, wherein the panel further
 comprises one or more biomarkers selected from a protein involved in a KEGG pathway selected
 from the group of complement and coagulation cascade, glycolysis/glycogenesis, prion disease,
 amino and nucleotide sugar metabolism, antigen processing and presentation, extracellular
 matrix-receptor interaction, focal adhesion, regulation of actin cytoskeleton or
 alanine/aspartate/glutamate metabolism.
- 25 5. The biomarker panel according to any one of claims 1 to 4, wherein the panel further
 comprises at least one, optionally two or more, biomarkers selected from any one of Tables 1, 2,
 3, 4, 5, 6, 7, 8 or 9 or fragments thereof.
- 30 6. The biomarker panel according to any one of claims 1 to 4 wherein the panel further comprises
 at least two or more, optionally at least three or more biomarkers selected from the group of
 Dynactin subunit 1, Cofilin-1, Peroxiredoxin-1, MARCKS-related protein, Moesin, Actin, Protein
 TMSB4XP4, ApoE, Gelsolin, Secretogranin, Albumin and complement proteins.
- 35 7. A method for diagnosing a neurocognitive disorder in a subject, the method comprising:
 - a) assaying a sample obtained from said subject for the biomarkers of the biomarker

panel according to any one of claims 1 to 6;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether that subject has a neurocognitive disorder by comparing said
5 concentration or amount of each of the biomarker of the biomarker panel in said sample with reference concentrations or amounts of said biomarkers.

8. A method for staging a neurocognitive disorder in a subject, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker
10 panel according to any one of claims 1 to 6;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining the stage of the neurocognitive disorder in said subject by comparing said
concentration or amount of each of the biomarkers of the biomarker panel in said sample with
15 reference concentrations or amounts of said biomarkers.

9. A method for assessing in a subject the likelihood of developing a neurocognitive disorder, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker
20 panel according to any one of claims 1 to 6;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether that subject is likely to develop a neurocognitive disorder by
comparing said concentration or amount of each of the biomarkers of the biomarker panel in said
25 sample with reference concentrations or amounts of said biomarkers.

10. The method of any one of claims 7 to 9, wherein the neurocognitive disorder is characterised by microglia activation.

30 11. The method according to any one of claims 7 to 10, wherein the neurocognitive disorder is selected from the group of mild cognitive impairment, Alzheimer's disease, vascular dementia, dementia with lewy bodies, fronto-temporal dementia or combinations thereof.

12. The method according to claim 11, wherein the neurocognitive disorder is Alzheimer's
35 disease.

13. A method for treating Alzheimer's disease in a subject, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarkers panel according to any one of claims 1 to 6;

5 b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

c) determining whether that subject has Alzheimer's disease by comparing said concentration or amount of each of the biomarkers in said sample with reference concentrations or amounts of said biomarkers;

10 d) administering to said subject an Alzheimer's disease treatment selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof.

14. A method for aiding the prognosis of a treatment for Alzheimer's disease in a subject, the method comprising:

a) assaying a sample obtained from said subject for the biomarkers of the biomarker panel according to any one of claims 1 to 6;

b) measuring in said sample the concentration or the amount of each of the biomarkers of said biomarker panel;

20 c) determining whether said treatment for Alzheimer's disease is successful by comparing said concentration or amount of each of the biomarker in said sample with reference concentrations or amounts of said biomarkers.

15. The method according to claim 14, wherein the treatment for Alzheimer's disease is selected from the group of memantine (e.g. Namenda ®), galantamine (e.g. Razadyne®), rivastigmine (e.g. Exelon®), donepezil (e.g. Aricept®), solanezumab, 5HT₅ antagonists or combinations thereof.

16. The method according to any one of claims 7 to 15, wherein the sample is selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof.

17. The method according to any one of claims 7 to 16, wherein the sample is CSF.

18. The method according to any one of claims 7 to 17, wherein the subject is a human subject.

19. The method according to claim 18, wherein the subject is a human subject previously diagnosed with mild cognitive impairment.

20. The method according to any one of claims 18 or 19, wherein the subject is a human subject
5 undergoing further clinical assessment of dementia.

21. The method according to any one of claims 7 to 20, wherein the assaying step a) and/or the measuring step b) comprise:

- 10 i) contacting said sample with one or more binding agents to each of said biomarkers of the biomarker panel; or
- ii) detecting in said sample autoantibodies specific to each of said biomarkers; or
- iii) detecting in said sample by mass spectrometry each of said biomarkers of the biomarker panel, optionally by previously labelling said sample with one or more isobaric reactive mass labels; or
- 15 iv) detecting in said sample by 2D gel electrophoresis each of said biomarkers of the biomarker panel; or
- v) any combinations of i), ii), iii) or iv).

22. The method according to claim 21, wherein the assaying is step a) and/or the measuring is
20 step b) comprise detecting one or more fragments of said biomarker in the biomarker panel.

23. The method according to claim 21 or claim 22, wherein the sample is immobilised on a solid support.

25 24. A method for identifying biomarkers in a sample obtained from a subject, wherein the biomarkers are suitable for diagnosing or staging Alzheimer's disease, wherein the method comprises using activate microglia cells (e.g. BV2 cells) and/or their culture media in mass spectrometry and/or wherein the biomarkers are identified in said sample by using activated microglia cells as a reference.

30

25. The method according to claim 24, wherein the biomarker panel comprises the biomarkers as defined in any one of claims 1 to 6.

26. The method of any one of claims 24 or 25, wherein said sample is selected from the group of
35 CSF, blood, serum or plasma.

27. A kit comprising reagents for assaying and/or measuring in a sample biomarkers of a biomarker panel as defined in any one of claims 1 to 6.

5 28. The kit according to claim 27, wherein the reagents comprise one or more binding agents which specifically bind to the biomarkers of the biomarker panels.

29. The kit according to claim 28, wherein the one or more binding agents are primary antibodies, wherein each primary antibody specifically binds to a different biomarkers of the biomarker panel.

10

30. The kit according to claim 29, wherein the reagents further comprise one or more secondary antibodies which specifically bind to said primary antibodies.

31. The kit according to claim 30, wherein the secondary antibodies are labelled.

15

32. The kit according to any one of claims 27 to 31, wherein said sample is selected from the group of cerebrospinal fluid (CSF), blood, plasma, serum, saliva, urine, tissue (e.g. brain tissue) or combinations thereof.

1/8

Fig. 1

10 20 30 40 50
MVKIVTVKTQ AYQDQKPG[T]S GLRKRVKVFQ SSANYAEN[FI] [Q]SIISTVEPA
* *

60 70 80 90 100
QRQEATLVVG G[D]GRFYM[K]EA IQLIARIAAA NGIGRLV[I]GQ NGILSTPAVS

110 120 130 140 150
CIIRKIKAI G IIL[T]ASHNP [G]GPNGDFGIK FNISNGGPAP EAITDKIFQI
*

160 170 180 190 200
SKTIEEYAVC PDLKVDLGVL GKQQFDLENK FKPFTVEIVD SVEAYATMLR

210 220 230 240 250
SIFDFSALKE LLSGPNRLKI [R]IDAMHGVVG PYVKKILCEE LGAPANSVAVN

260 270 280 290 300
CVPLEDFGGH HP[D]PNLTYAA DLVETMKSGE HDFGAAFDGD [G]DRNMILGKH

310 320 330 340 350
GFFVNPSDSV AVIAANIFSI PYFQQTGVR[G] FARSMPTSGA LDRVASATKI
*

360 370 380 390 400
ALYETPTGWK FFGNLMASK LSLCGE[E]SFG TGSDHIRE[E]KD GLWAVLAWLS
*

410 420 430 440 450
ILATRKQSVE DILKDHQK[Y] GRNFFTRYDY EEVEAEGANK MMKDLEALMF
*

460 470 480 490 500
DRSFVGKQFS ANDKVYTVEK ADNFEYSDPV DGSISRNOGL RLIFTDGSRI
*

510 520 530 540 550
[V]FRLSGTGSA GATIR[L]YIDS YEKDVAKINQ DPQVMLAPLI SIALKVSQIQ
*

560
ERTGRTAPTV IT

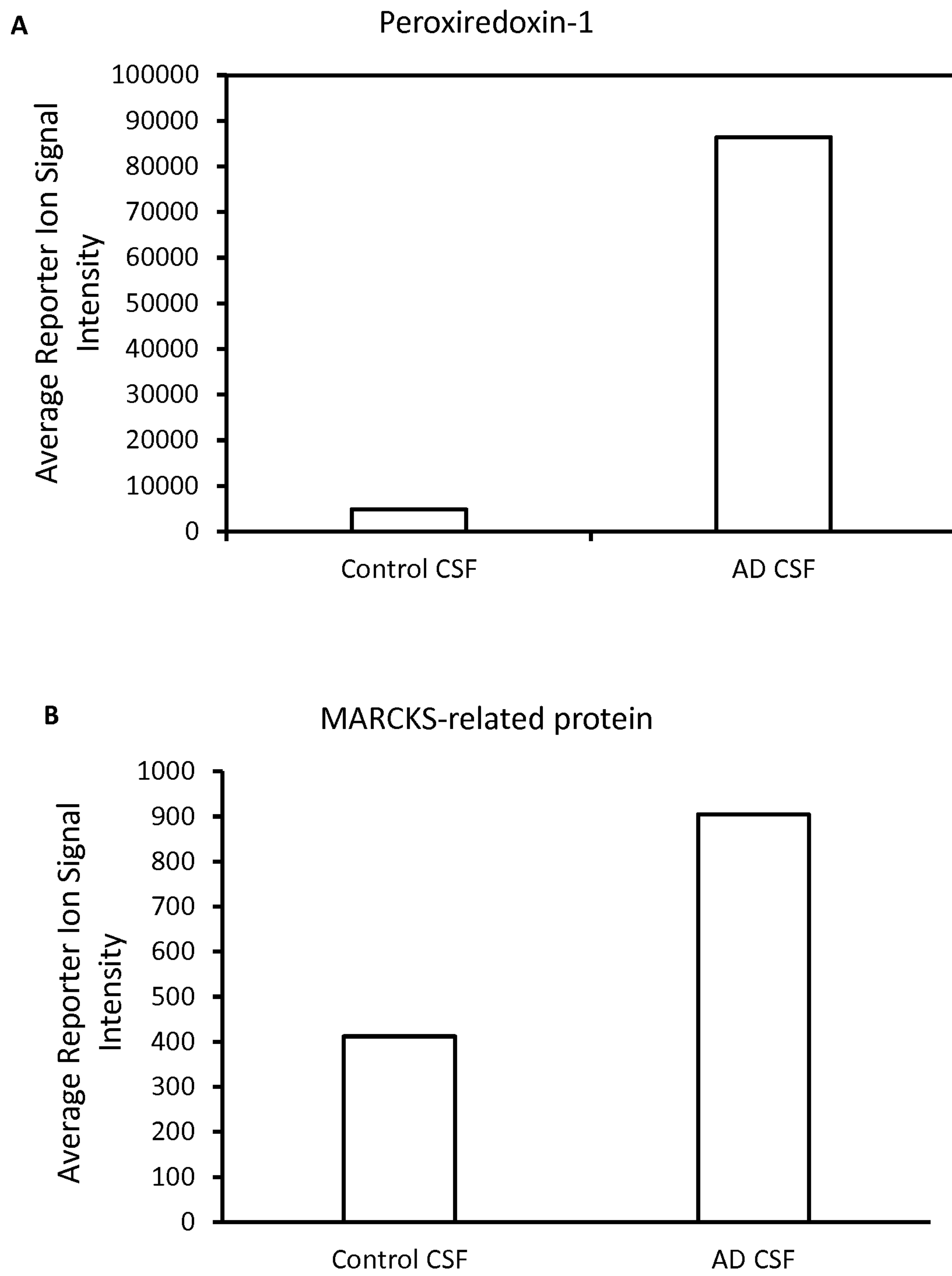
2/8

Fig. 2

10 20 30 40
MSDKPDMAEI EKFDKSKLKK TETQEKNP LP SKETIEQEKQ AGES
* * *

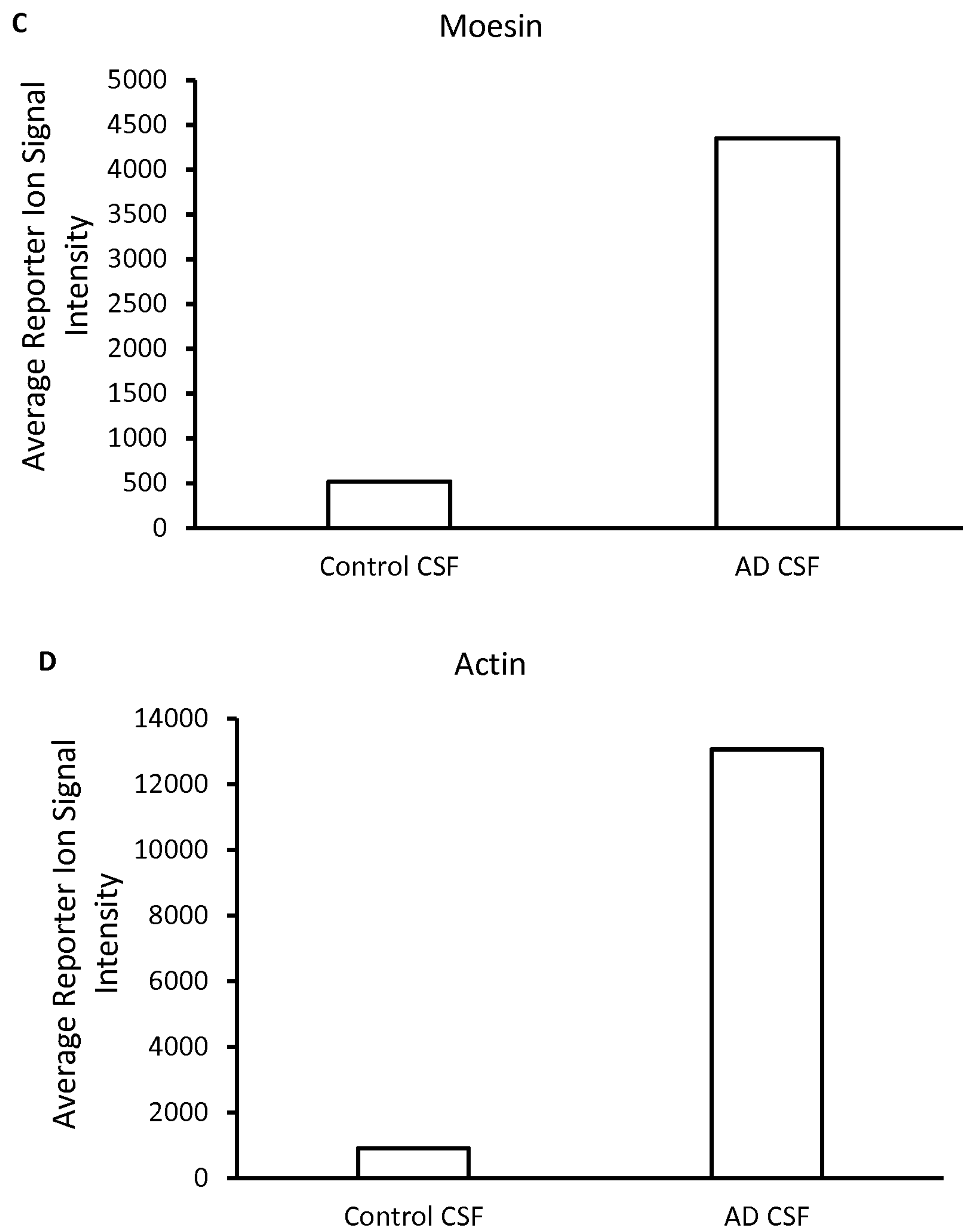
3/8

Fig. 3



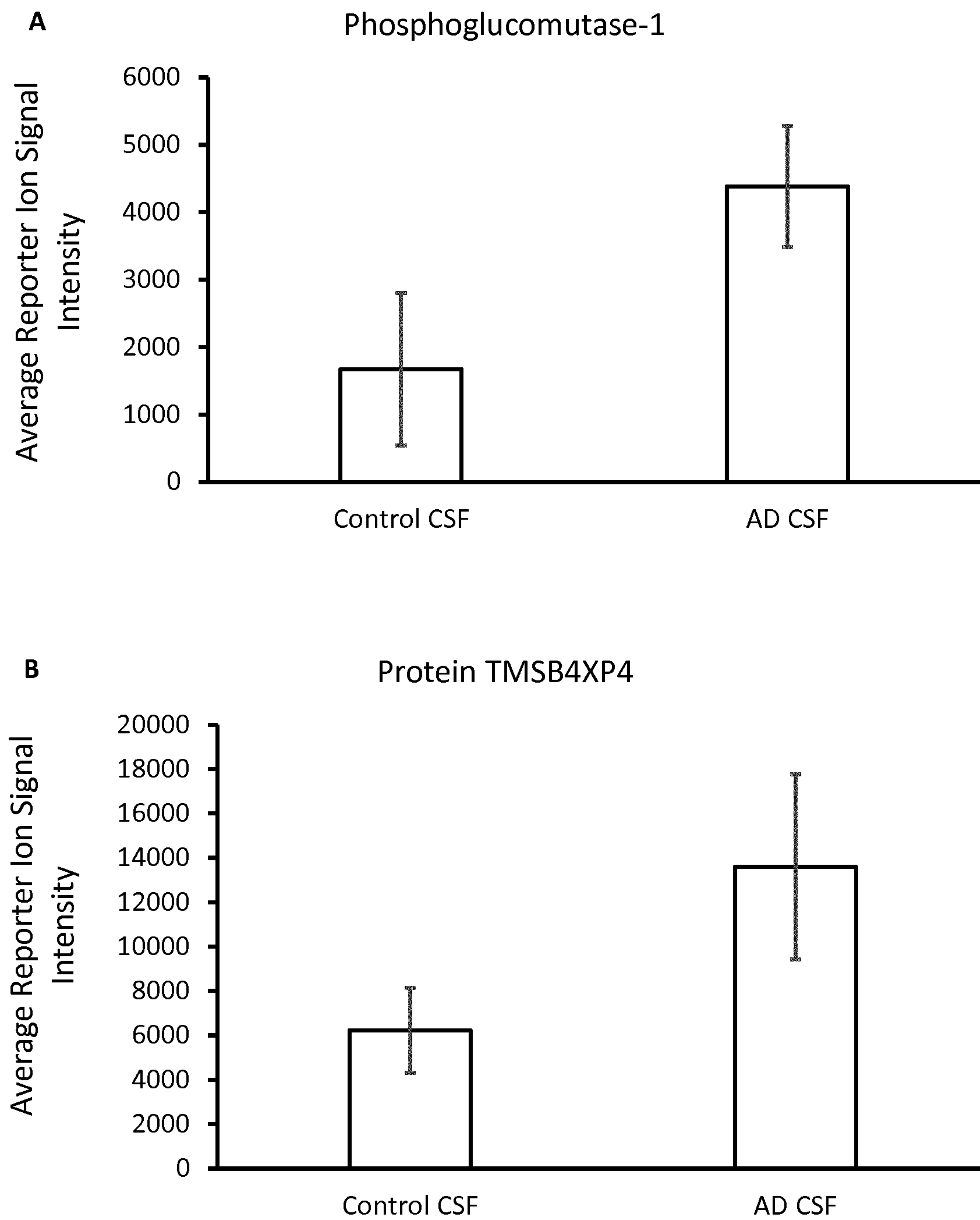
4/8

Fig. 3 (continued)



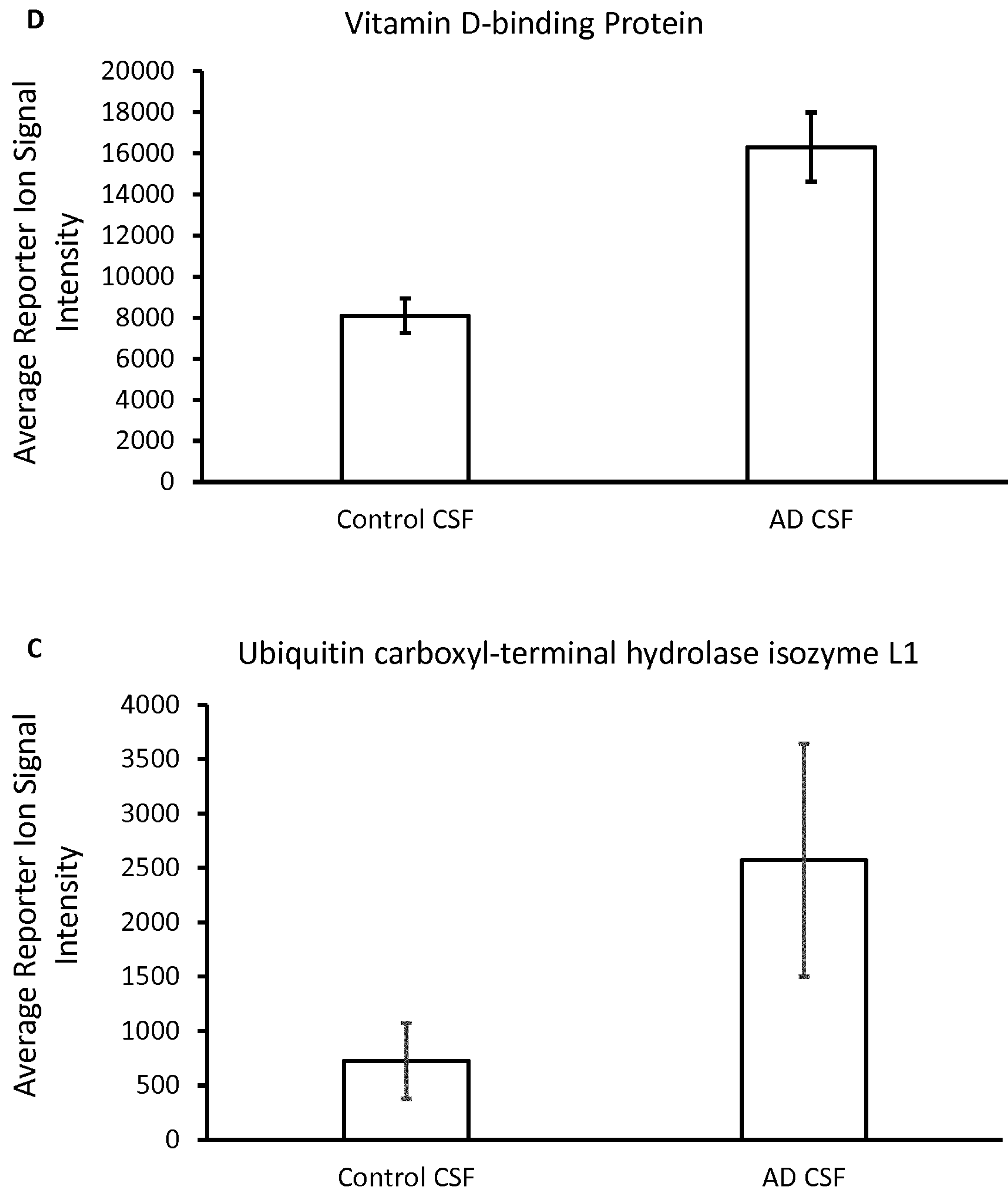
5/8

Fig. 4



6/8

Fig. 4 (continued)



7/8

Fig. 5

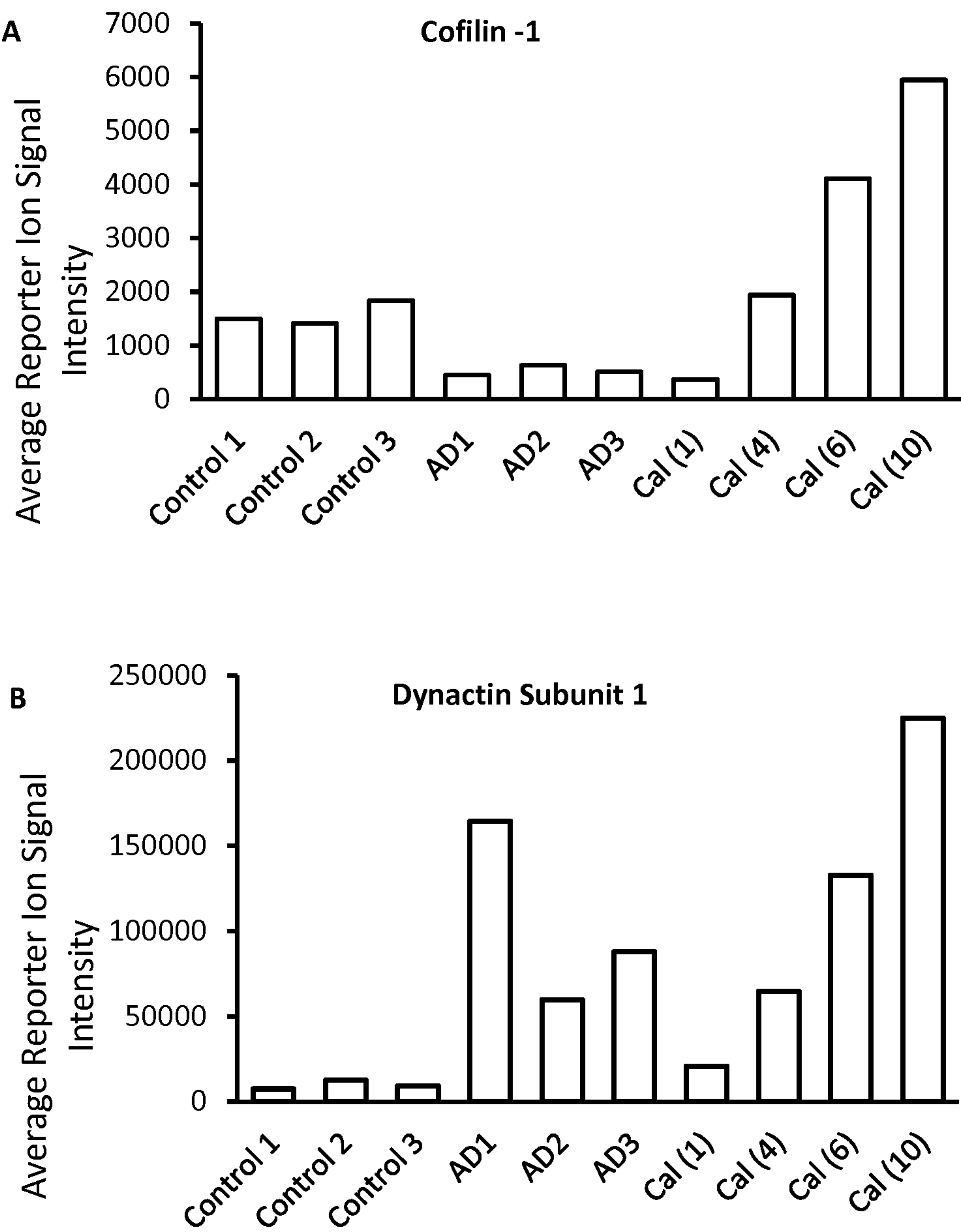


Fig. 6

