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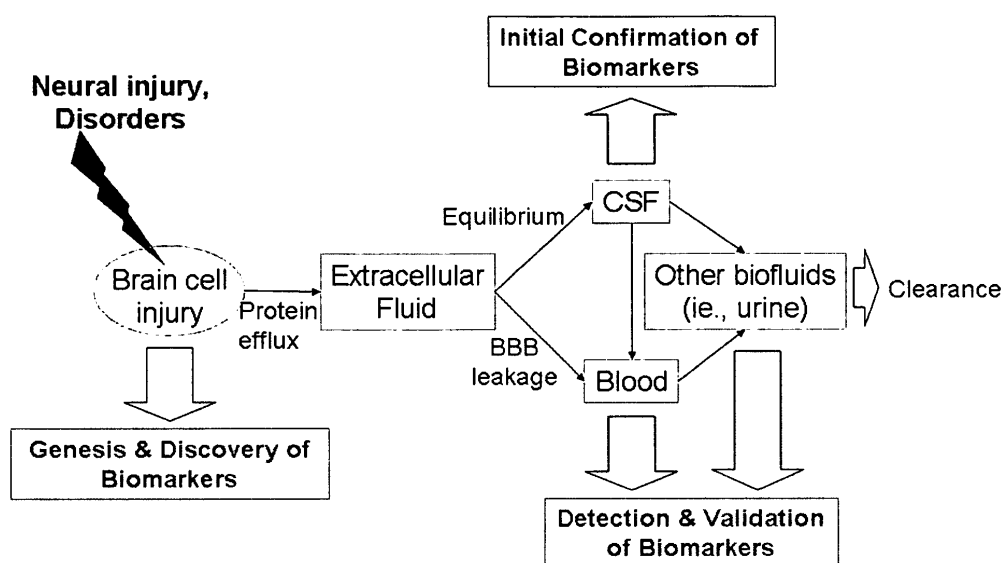
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(54) **Neural proteins as biomarkers for nervous system injury and other neural disorders**

(57) The present invention identifies biomarkers that are diagnostic of nerve cell injury and/or neuronal disorders. Detection of different biomarkers of the invention

are also diagnostic of the degree of severity of nerve injury, the cell(s) involved in the injury, and the subcellular localization of the injury.



**FIGURE 1**



## EUROPEAN SEARCH REPORT

Application Number  
EP 10 00 1581

| DOCUMENTS CONSIDERED TO BE RELEVANT  |   |  |   |
|--|---|--|---|
| Category   | Citation of document with indication, where appropriate, of relevant passages   | Relevant to claim                                  | CLASSIFICATION OF THE APPLICATION (IPC)             |
| A,P  | WO 2005/004794 A2 (ALNYLAM PHARMACEUTICALS INC [US]; MAYO FOUNDATION [US]; BUMCROT DAVID) 20 January 2005 (2005-01-20)<br>* abstract *<br>* claims 13, 21, 26 *   | 1-26   | INV.<br>G01N33/53<br>C12Q1/68                       |
| X  | JP 2003 070498 A (PHARMA DESIGN INC) 11 March 2003 (2003-03-11)<br>* abstract *   | 1-17,<br>22-26                                     |   |
| A  | WO 03/019181 A2 (SYN X PHARMA INC [CA]) 6 March 2003 (2003-03-06)<br>* claims 1-5 *   | 1-26   |   |
| T  | PAPA LINDA ET AL: "Ubiquitin C-terminal hydrolase is a novel biomarker in humans for severe traumatic brain injury." CRITICAL CARE MEDICINE JAN 2010 LNKD-PUBMED:19726976, vol. 38, no. 1, January 2010 (2010-01), pages 138-144, XP009132536<br>ISSN: 1530-0293<br>* the whole document *                  | 1-26   |   |
| T  | LIU MING C ET AL: "Ubiquitin C-terminal hydrolase-L1 as a biomarker for ischemic and traumatic brain injury in rats." THE EUROPEAN JOURNAL OF NEUROSCIENCE FEB 2010 LNKD- PUBMED:20384815, vol. 31, no. 4, February 2010 (2010-02), pages 722-732, XP002579053<br>ISSN: 1460-9568<br>* the whole document * | 1-26   | TECHNICAL FIELDS SEARCHED (IPC)<br><br>G01N<br>C12Q |
| The present search report has been drawn up for all claims   |   |  |   |
| Place of search<br>Munich  |   | Date of completion of the search<br>27 August 2010 | Examiner<br>Weijland, Albert                        |
| CATEGORY OF CITED DOCUMENTS<br>X : particularly relevant if taken alone<br>Y : particularly relevant if combined with another document of the same category<br>A : technological background<br>O : non-written disclosure<br>P : intermediate document<br>T : theory or principle underlying the invention<br>E : earlier patent document, but published on, or after the filing date<br>D : document cited in the application<br>L : document cited for other reasons<br>& : member of the same patent family, corresponding document |   |  |   |

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EPO FORM 1503 03.82 (P04C01)



## EUROPEAN SEARCH REPORT

Application Number  
EP 10 00 1581

| DOCUMENTS CONSIDERED TO BE RELEVANT   |  |  |   |
|---|--|--|---|
| Category  | Citation of document with indication, where appropriate, of relevant passages  | Relevant to claim                                  | CLASSIFICATION OF THE APPLICATION (IPC) |
| X   | SMITH D H ET AL: "Protein accumulation in traumatic brain injury"<br>NEUROMOLECULAR MEDICINE, HUMANA PRESS, US LNKD- DOI:10.1385/NMM:4:1-2:59,<br>vol. 4, no. 1-2,<br>1 October 2003 (2003-10-01), pages 59-72,<br>XP008097564<br>ISSN: 1535-1084<br>* abstract *<br>* page 64, right-hand column, last paragraph *<br>* page 65, right-hand column, paragraph 2 * | 22-26  | TECHNICAL FIELDS SEARCHED (IPC)         |
| X   | -----<br>ARAKI MASASUKE ET AL: "Developmentally regulated expression of Neuro-p24 and its possible function in neurite extension."<br>NEUROSCIENCE RESEARCH DEC 2002 LNKD-PUBMED:12445626,<br>vol. 44, no. 4, December 2002 (2002-12), pages 379-389, XP002598262<br>ISSN: 0168-0102<br>* abstract *   | 22-26  |   |
| X   | -----<br>MILLER L P ET AL: "Excitatory amino acid receptor subtype binding following traumatic brain injury."<br>BRAIN RESEARCH 27 AUG 1990 LNKD-PUBMED:1964103,<br>vol. 526, no. 1,<br>27 August 1990 (1990-08-27), pages 103-107, XP002598263<br>ISSN: 0006-8993<br>* abstract *<br>* page 325, paragraph 3 - paragraph 4 *<br>-----<br>-/--                     | 22-26  |   |
| The present search report has been drawn up for all claims  |  |  |   |
| Place of search<br>Munich   |  | Date of completion of the search<br>27 August 2010 | Examiner<br>Weijland, Albert            |
| <p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone<br/>Y : particularly relevant if combined with another document of the same category<br/>A : technological background<br/>O : non-written disclosure<br/>P : intermediate document</p> <p>T : theory or principle underlying the invention<br/>E : earlier patent document, but published on, or after the filing date<br/>D : document cited in the application<br/>L : document cited for other reasons<br/>-----<br/>&amp; : member of the same patent family, corresponding document</p> |  |  |   |

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EPO FORM 1503 03 82 (P04C01)



## EUROPEAN SEARCH REPORT

Application Number  
EP 10 00 1581

| DOCUMENTS CONSIDERED TO BE RELEVANT  |   |   |   |
|--|---|---|---|
| Category   | Citation of document with indication, where appropriate, of relevant passages   | Relevant to claim   | CLASSIFICATION OF THE APPLICATION (IPC) |
| X  | <p>HANSEN L A ET AL: "Frontal cortical synaptophysin in Lewy body diseases: relation to Alzheimer's disease and dementia."<br/>JOURNAL OF NEUROLOGY, NEUROSURGERY, AND PSYCHIATRY MAY 1998 LNKD- PUBMED:9598683, vol. 64, no. 5, May 1998 (1998-05), pages 653-656, XP002598264<br/>ISSN: 0022-3050<br/>* abstract *</p> <p style="text-align: center;">-----</p> | 22-26   |   |
|  |   |   | TECHNICAL FIELDS SEARCHED (IPC)         |
|  |   |   |   |
| The present search report has been drawn up for all claims   |   |   |   |
| Place of search<br><b>Munich</b>   |   | Date of completion of the search<br><b>27 August 2010</b> | Examiner<br><b>Weijland, Albert</b>     |
| <p><b>CATEGORY OF CITED DOCUMENTS</b></p> <p>X : particularly relevant if taken alone<br/>Y : particularly relevant if combined with another document of the same category<br/>A : technological background<br/>O : non-written disclosure<br/>P : intermediate document</p> <p>T : theory or principle underlying the invention<br/>E : earlier patent document, but published on, or after the filing date<br/>D : document cited in the application<br/>L : document cited for other reasons<br/>.....<br/>&amp; : member of the same patent family, corresponding document</p> |   |   |   |

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EPO FORM 1503 03/82 (P04C01)



Application Number

EP 10 00 1581

**CLAIMS INCURRING FEES**

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

**LACK OF UNITY OF INVENTION**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION  
SHEET B**

Application Number

EP 10 00 1581

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-26(partially)

methods for determining the presence of traumatic brain injury using ubiquitin C-terminal hydrolase L1 (UCH-L1) as biomarker and compositions and kits therefore

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2. claims: 1-16, 19, 21-26(all partially)

methods for determining the presence of traumatic brain injury using p24 as biomarker and compositions and kits therefore

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3. claims: 1-16, 18, 21-26(all partially)

methods for determining the presence of traumatic brain injury using alpha-synuclein as marker and compositions and kits therefore

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4. claims: 1-16, 18, 21-26(all partially)

methods for determining the presence of traumatic brain injury using beta-synuclein as marker and compositions and kits therefore

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5. claims: 1-16, 20-26(all partially)

methods for determining the presence of traumatic brain injury using synaptophysin-1 as biomarker and compositions and kits therefore

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6. claims: 1-16(partially)

methods for determining the presence of traumatic brain injury using NMDA-receptor units as biomarker and compositions and kits therefore

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**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 10 00 1581

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

27-08-2010

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|---------------------|----------------------------|---------------------|
| WO 2005004794 A2                          | 20-01-2005          | AU 2004255557 A1           | 20-01-2005          |
|   |                     | CA 2542232 A1              | 20-01-2005          |
|   |                     | EP 1635763 A2              | 22-03-2006          |
|   |                     | JP 2007528367 T            | 11-10-2007          |
| -----                                     |                     |                            |                     |
| JP 2003070498 A                           | 11-03-2003          | NONE                       |                     |
| -----                                     |                     |                            |                     |
| WO 03019181 A2                            | 06-03-2003          | AU 2002325105 A1           | 10-03-2003          |
|   |                     | US 2006051814 A1           | 09-03-2006          |
|   |                     | US 2003040660 A1           | 27-02-2003          |
| -----                                     |                     |                            |                     |

|                |  |         |            |
|----------------|--|---------|------------|
| 专利名称(译)        | 神经蛋白作为神经系统损伤和其他神经疾病的生物标志物  |         |            |
| 公开(公告)号        | <a href="#">EP2207033A3</a>  | 公开(公告)日 | 2010-11-03 |
| 申请号            | EP2010001581   | 申请日     | 2005-04-15 |
| [标]申请(专利权)人(译) | 佛罗里达大学研究基金会有限公司  |         |            |
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| 当前申请(专利权)人(译)  | 佛罗里达州研究基金会，Inc.的大学.<br>BANYAN生物标志物，INC.                                |         |            |
| [标]发明人         | HAYES RONALD<br>WANG KA WANG KEVIN<br>LIU MING CHEN<br>OLI MONIKA      |         |            |
| 发明人            | HAYES, RONALD<br>WANG, KA-WANG, KEVIN<br>LIU, MING-CHEN<br>OLI, MONIKA |         |            |
| IPC分类号         | G01N33/53 C12Q1/68 G01N33/537 G01N33/543 G01N33/68                     |         |            |
| CPC分类号         | C12Q1/6883 G01N33/6896 G01N2800/28 G01N2800/52                         |         |            |
| 优先权            | 60/562944 2004-04-15 US  |         |            |
| 其他公开文献         | EP2207033B1<br>EP2207033A2   |         |            |
| 外部链接           | <a href="#">Espacenet</a>  |         |            |

#### 摘要(译)

本发明鉴定了诊断神经细胞损伤和/或神经元病症的生物标志物。检测本发明的不同生物标志物还可以诊断神经损伤的严重程度，涉及损伤的细胞和损伤的亚细胞定位。

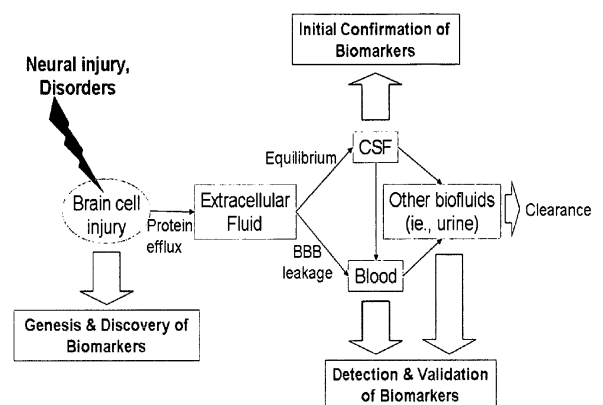


FIGURE 1