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[Continued on next page]

(54) Title: BIOMARKERS OF NEURODEGENERATIVE DISEASE

FIGURE 1

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1 gagctggggg ggggcagggg ggggagagtc gatccagtct ctgactgtga
gagcaagcag
61 ccagaagcag actccttaat tccaggggac ctagagctag agcctgcagc
aatggcctgg
121 gacctaaagg tgaagatgct ggggggtaac gatttcctgg tgtccgtgac
taactccatg
181 acggtgtcag aactgaagaa gcagattgcc cagaagattg gtgtgccggc
tttccagcag
241 cgctggccc accaaactgc agtgctccag gacggtctta cctttccag
tctgggtctg
301 ggtcccagca gcacagtgat gctagtggta cagaactgca gcgagcctct
gagcatcctg
361 gtgaggaacg aaaggggcca cagcaacatc tatgaggtct ttctgacgca
gactgtagac
421 acgcttaaga agaaggtgtc cagcgggaaca agtcacgaag accagtctctg
gctgagcttc
481 gagggaaggc ccatggagga caaggagctg ctgggggagat atggcctaaa
gccccagtgc
541 acagtgatca agcatttgct cctgaggggt gggggagggg accagtgtgc
ctaaggcccc
601 catccagagc cagtgttggt tataaaagat gatggggggg ggggtatgga
ggacttttgg
661 gatagcattg gaaatgtaaa cgaggaaaat acctaattag aaaaaaatc
aaaaaaaaa
721 aaaagctc

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(57) Abstract: The present invention provides biomarkers and diagnostic methods employing such biomarkers based on the discovery of genes that have a two-fold or greater difference in gene expression in the spinal cord of a pre-symptomatic mouse model of amyotrophic lateral sclerosis. Such biomarkers and diagnostic methods are useful for early detection of neural cell injury and death in acute and degenerative disease.

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A. CLASSIFICATION OF SUBJECT MATTER IPC: G01N 33/558(2006.01),33/561(2006.01),33/543(2006.01),33/557(2006.01);A61K 49/00(2006.01);C07H 21/04(2006.01) USPC: 436/514,516,517,518;424/9.1;536/24.3 According to International Patent Classification (IPC) or to both national classification and IPC												
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 436/514, 516,517,518; 424/9.1; 536/24.3 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet												
C. DOCUMENTS CONSIDERED TO BE RELEVANT												
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X	Lukas et al. Mol.Cell. Proteomics 2006. 5:1233-1244, especially p. 1233, abstract; p. 1234-1240.	1, 4-9, 19-20 and 23-24										
X	Perrin et al. J. Neurochem. 2006: 98: 1959-1972, especially p. 1959, abstract; p. 1960-1961; p.1969-1970.	10, 13-18, 21-22 and 25-27										
A	US2007/0203083 (Mootha et al., Aug 30, 2007) the whole document.	1-29										
A	US2006/0073496 (O'Toole et al., Apr 6, 2006) especially p. 4-7; p.13-15; p. 93-138.	1-29										
☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.												
* Special categories of cited documents: <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone											
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art											
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family											
"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 24 July 2008 (24.07.2008)		Date of mailing of the international search report 11 AUG 2008										
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer /CYW/ Chang-Yu Wang Telephone No. 571-272-1600										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US08/02035

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
 2. ☒ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
 3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
 4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US08/02035

Continuation of B.FIELDS SEARCHED - Item Electronic data base consulted during the international search (name of data base and, where practicable, search terms used):
STN: Biosis, Biotechds, Embase, CAPLUS, Medline, USPATFULL, search term: SOD or SOD1, amyotrophic lateral sclerosis, Alzheimer, Parkinson, neurodegenerative or neurodegeneration, Isg15, Usp18, ifi202, Iigp1, Ifi27, Ifit3, Oasl2, Ifit1, Rsad2, Ifi44, Isg15, Cxc110, Gbp2, Socs3, Irf8, Oas1a, Irgm, B2m, Psmb8, Igtp, Isgf3g, Ifitm3, Stat1, Ifih1, Iigp2, Ifit2, Samhd1, Clec7a, ubiquitin speciifc peptide 18, interfeon-a-inducible protein.