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(54) Title: DIAGNOSTIC MARKERS OF STROKE AND CEREBRAL INJURY AND METHODS OF USE THEREOF

(57) Abstract: The present invention relates to methods for the diagnosis and evaluation of stroke and transient ischemic attacks. A variety of markers are disclosed for assembling a panel for such diagnosis and evaluation. In various aspects, the invention provides methods for early detection and differentiation of stroke types and transient ischemic attacks, for determining the prognosis of a patient presenting with stroke symptoms, and identifying a patient at risk for cerebral vasospasm. Invention methods provide rapid, sensitive and specific assays to greatly increase the number of patients that can receive beneficial stroke treatment and therapy, and reduce the costs associated with incorrect stroke diagnosis.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/38225

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A61K 49/00**(2006.01),**39/395**(2006.01);**C07H 21/04**(2006.01)

USPC: 424/9.1,130.1;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. : 424/9.1, 130.1; 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 --- Y	Zhuo et al. HBO suppresses Nogo-A, NgR, or RhoA expresion in the cerebral cortex after global ischemia. BBRC. (2003). vol. 309, pages 368-376. See throughout.	1, 23-30 --- 2-7, 9-22
Y	Shirasaki et al. Serum s-100b protein as a biomarker for the assessment of neuroprotectants. Brain Research. 2004. vol., 1021, pages 159-166. see throughout.	1-5, 10, 17-30
Y	Ma et al. RAGE is expressed in pyramidal cells of the hippocampus following moderate hypoxic-ischemic brain injury in rats. Brain Research. 2003. vol. 966, pages 167-174. See	6-7, 11-12
Y	Hatfield et al. CSF neuron-specific enolase as a quantitative marker of neuronal damage in a rat stroke model. Brain Research. 17 April 1992, vol. 577, Abstract only. See abstract.	13-16
Y	Ceoroli et al. Nitric Oxide production and perivascular tyrosine nitration following focal ischemia in neonatal rat. J. Neurochemistry. 1998. vol. 70, pages 2516-2525.	13-16
Y	Eikelboom et al. C-reactive protein in ischemic stroke and its etiologic subtypes. Journal of Stroke and Cerebrovascular diseases. 2003. 12, 74-81. see title and abstract.	13-16

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Clark et al. Increased gelatinase A (MMP-2) and gelatinase B (MMP-9) activities in human brain after focal ischemia. Neuroscience Letters. 1997, vol. 238, pages 53-56. see title and abstract.	13-16
Y	Barber et al. Hemostatic function and progressing ischemic stroke: D-dimer predicts early clinical progression. Stroke. 2004. , vol. 35, pages 1421-1425.	13-16

Continuation of B. FIELDS SEARCHED Item 3:
pubmed, east: ischemia and s-100b, and nitrotyrosine, and NOGO receptor, and C-reactive protein, and RAGE, and caspase-3, and MMP-2, and D-dimer, and enolase.