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(54) Title: DERIVATION OF NEURAL STEM CELLS FROM EMBRYONIC STEM CELLS AND METHODS OF USE THEREOF

(57) Abstract: Provided is a method for the derivation of neural stem cells (NSCs) from embryonic stem cells (ESCs) and the use of the NSCs for treatment of various neural disorders. The NSCs that are derived from the ESCs are tissue-specific multipotent NSCs with a stable growth rate, unlimited self-renewal capacity, and a predictable differentiation profile. Being both non-tumorigenic and engraftable, the NSCs of the present invention have utility in repopulation stroke-damaged tissue. The NSCs of the present invention may be differentiated to produce tyrosine-hydroxylase expressing neurons, which may be used as a source of dopaminergic neurons for subjects suffering from a condition characterized by dopaminergic dysfunction, such as Parkinson's disease.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/77407

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 5/08 (2008.04)

USPC - 435/368

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)

USPC: 435/368

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 435/377,366,325 (See Search Terms Below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWest: PGPB, USPT, USOC, EPAB, JPAB; Google Patents, Google Scholar, Google; neural stem cells, homogeneous, embryonic stem cells, EGF, FGF, LIF, stroke, striatum, human, mammal, plating, spheres, primary,secondary, container, stem cell, marker, nestin, poly-L-ornithine, astrocytes, oligodendrocytes, neurons, MAP-2, tu

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0221479 A1 (Nakayama et al.) 06 October 2005 (06.10.2005), para [0006], [0008], [0014]-[0015], [0018], [0040], [0067], [0135]- [0136], [0191]	1 and 2
Y		3-21
Y	US 2005/0255589 A1 (Reubinoff) 17 November 2005 (17.11.2005), para[0005], [0028]-[0030], [0037], [0040]-[0043], [0080], [0154], [0117], [0183], [0194], [0198], [0206], [0219], [0224], [0226], [0287], [0289]-[0291], [0295], [0301]	3-6 and 22-60
Y	US 2007/0155012 A1 (Privat et al.) 05 July 2007 (05.07.2007), abstract; para [0023], [0025], [0031], [0056]-[0059], [0072], [0191]	7-21
Y	US 2005/0074880 A1 (Sang et al.) 07 April 2005 (07.04.2005), para [0013]	12
Y	US 6,294,346 B1 (Weiss et al.) 25 September 2001 (25.01.2001), col 20, ln 23-25; col 20, ln 50-54, col 60, Table II	19, 21
Y	Engele et al. Conditioned media derived from glial cell lines promote survival and differentiation of dopaminergic neurons in vitro: role of mesencephalic glia. Journal of Neuroscience 1991, 30:359-371, abstract; pg 360, col 2, para 2; pg 359, col 2, para 1; pg 360, col 1, para 1; pg 365, col 2, para 1	22-60
Y	US 5,981,165 A (Weiss et al.) 09 November 1999 (09.11.1999), col 8, ln 47-48	25, 34, and 45
Y	US 2006/0194315 A1 (Condie et al.) 31 August 2006 (31.08.2006), para [0090]	28-31, 33-36, 48-50 and 55-60

☒ Further documents are listed in the continuation of Box C.

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"P" document published prior to the international filing date but later than the priority date claimed

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"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

"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

"&" document member of the same patent family

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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	WO/2004/103394 A2 (Zou) 02 December 2004 (02.12.2004), pg 9, ln 7-9.	30-31, 35-36, 50 and 55-60
Y	US 6,284,539 B1 (Bowen et al.) 04 September 2001 (04.09.2001), col 1, ln 30-32; col 15, ln 38-39; col 16, ln 19-22; col 17, ln 1-6.	59-60