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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ASTROCYTE MODULATED GENES AND USES THEREOF

(57) **Abstract:** The present invention relates to Astrocyte Modulated Genes (*AMGs*). *AMGs* are genes whose expression are modulated in human astrocytes grown in primary cell culture following the exposure of these cells to either the human immunodeficiency virus HIV-1 or to the HIV-1 protein gp120. *AMGs* comprise both Astrocyte Enhanced Genes (*AEGs*) and Astrocyte Suppressed Genes (*ASGs*). Thus, the present invention further relates to Astrocyte Enhanced Genes (*AEGs*), the expression of which are up-regulated in human astrocytes grown in primary cell culture that are exposed to either the human immunodeficiency virus HIV-1 or to the HIV-1 protein gp120, and to Astrocyte Suppressed Genes (*ASGs*), the expression of which are downregulated in human astrocytes grown in primary cell culture that are exposed to either the human immunodeficiency virus HIV-1 or to the HIV-1 protein gp 120. Because they may play a role in HIV-associated dementia ("HAD"), *AMGs* may be used as markers in methods for screening for drugs that treat or prevent HAD.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/11887

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 15/12

US CL : 536:23.5; 435/320.1

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. : 536/23.5; 435/69.1, 320.1, 325, 455

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)

NCBI BLAST, WEST, PubMed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	STRAUSBERG et al. Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences. Proceedings of the National Academy of Sciences, USA. December 2002, Vol. 99, No. 26, pages 16899-16903.	1, 4, 7, 10, 13, 16, 55, and 58
A, T	Database NCBI on STN, GenBank Accession BC045642, "Homo sapiens LYRIC/3D3, mRNA (cDNA clone MGC:41931 IMAGE:5298467), complete cds.", June 2004.	1, 4, 7, 10, 13, 16, 55, and 58
A, T	GenBank Accession AX780141, "Sequence 2298 from Patent WO03039443," July 2003.	1, 4, 7, 10, 13, 16, 55, and 58
X, T	SUTHERLAND et al. 3D3/lyric: a novel transmembrane protein of the endoplasmic reticulum and nuclear envelope, which is also present in the nucleolus. Experimental Cell Research. March 2004, Vol. 294, No. 1, pages 94-105.	1, 4, 7, 10, 13, 16, 55, and 58
X, T	Database NCBI on STN, GenBank Accession AF501310, "Homo sapiens LYRIC/3D3 mRNA, complete cds.," March 2004.	1, 4, 7, 10, 13, 16, 55, and 58



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:		"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier application or patent published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/11887

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

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

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 41-49
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:
These claims contain defects under Article 17(2)(a) (the claims are dependent claims that depend from themselves or from dependant claims that depend from themselves). Thus, no meaningful search of the claims can be carried out.
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

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 an additional fee, this Authority did not invite payment of any additional fee.
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.: 1,4,7,10,13,16,55 and 58

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/11887

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I, claim(s) 1, 4, 7, 10, 13, 16, 55, and 58, drawn to nucleic acids of SEQ ID NO: 1 and compositions thereof.

Group II, claim(s) 2, 5, 6, 11, 14, 17, 56, and 59, drawn to drawn to nucleic acids of SEQ ID NO: 3 and compositions thereof.

Group III, claim(s) 3, 6, 9, 12, 15, 18, 57, and 60, drawn to drawn to nucleic acids of SEQ ID NO: 4 and compositions thereof.

Group IV, claim(s) 19, 22, 25, 32, 35, and 38, drawn to AEG-1 proteins and peptides.

Group V, claim(s) 20, 23, 33, and 36, drawn to AEG-11 proteins and peptides.

Group VI, claim(s) 21, 24, 34, and 37, drawn to ASG-1 proteins and peptides.

Group VII, claim(s) 26, and 29, drawn to anti-AEG-1 antibodies.

Group VIII, claim(s) 27, and 30, drawn to anti-AEG-11 antibodies.

Group IX, claim(s) 28 and 31, drawn to anti-ASG-1 antibodies.

Group X, claim(s) 39, 50, and 54, drawn to methods for screening for agents that prevent or inhibit HIV-1 associated dementia comprising determining the effect of a test agent on the expression level of an AEG.

Group XI, claim(s) 40 and 51, drawn to methods for screening for agents that prevent or inhibit HIV-1 associated dementia comprising determining the effect of a test agent on the expression level of an ASG.

Group XII, claim(s) 52 and 53, drawn to methods for screening for agents that prevent or inhibit HIV-1 associated dementia comprising determining the effect of a test agent on the glutamate transport activity.

Group XIII, claim(s) 61, drawn to transgenic animals comprising an AEG-1 transgene operably linked to a heterologous promoter.

Group XIV, claim(s) 62, drawn to drawn to transgenic animals comprising an AEG-11 transgene operably linked to a heterologous promoter.

Group XV, claim(s) 63, drawn to drawn to transgenic animals comprising an ASG-1 transgene operably linked to a heterologous promoter.

The inventions listed as Groups I-XV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the inventions each relate to a different composition comprising a molecule that performs different functions or has different effects; or to methods not relating to the making or use of the claimed compositions; or to transgenic animals, each of which comprises a different transgene.

In particular, the inventions of Groups I-III, Groups IV-VI, and Groups VII-IX, each relate to different classes of molecules. Each of these classes of molecules has a different structure, a performs a different function. These inventions therefore share no common special technical feature.

The inventions of each of Groups I and IV, Groups II and V, and Groups III and VI each relate to inventions relating to the sequences, and products of a different gene. Each of these gene are disclosed in the application as having a different structure (see the sequence), a different mode of operation (see, Appl., page 7, lines 4-15, and pages 12-13). The inventions therefore lack a common special technical feature.

The inventions of Groups X-XII do not relate to methods of using or making the claimed compositions. Further, each of these methods has a different mode of operation from the other methods. They therefore share no common special technical feature either with each other, or with the claimed compositions.

The inventions share no common special technical feature, and therefore lack unity.