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(54) Title: DIAGNOSIS AND TREATMENT METHODS RELATED TO AGING (8A)

(57) Abstract: Mouse genes differentially expressed in comparisons of gene expression in growth hormone receptor/binding protein gene-disrupted mouse livers and normal mouse livers have been identified, as have corresponding human genes and proteins. The human molecules, or antagonists thereof, may be used for protection against faster-than-normal biological aging, or to achieve slower-than-normal biological aging. The human molecules may also be used as markers of biological aging, to retard biological aging, or to treat age-related diseases.

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

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)
IPC 7 C12Q

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 practical, search terms used)
EPO-Internal, BIOSIS, Sequence Search, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MERCHED A ET AL: "APOLIPOPROTEIN AIV CODON 360 MUTATION INCREASES WITH HUMAN AGING AND IS NOT ASSOCIATED WITH ALZHEIMER'S DISEASE" NEUROSCIENCE LETTERS, LIMERICK, IE, vol. 242, no. 2, 13 February 1998 (1998-02-13), pages 117-119, XP000863724 ISSN: 0304-3940 the whole document ----- -/--	1-3, 17-31

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"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)

"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

"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

"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

Date of the actual completion of the international search	Date of mailing of the international search report
10 January 2005	28 -06- 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bort, S

INTERNATIONAL SEARCH REPORT

Inter[redacted]nal Application No
PCT/US2004/021944

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MICHIKAWA Y ET AL: "Aging-dependent large accumulation of point mutations in the human mtDNA control region for replication" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, 22 October 1999 (1999-10-22), pages 774-779, XP002179334 ISSN: 0036-8075 the whole document	1-3, 17-31
X	LIO D ET AL: "Gender-specific association between -1082 IL-10 promoter polymorphism and longevity" GENES AND IMMUNITY, vol. 3, no. 1, February 2002 (2002-02), pages 30-33, XP008039832 ISSN: 1466-4879 the whole document	1-3, 17-31
X	MOCCHEGIANI EUGENIO ET AL: "MTmRNA gene expression, via IL-6 and glucocorticoids, as potential genetic marker of immunosenescence: Lessons from very old mice and humans" EXPERIMENTAL GERONTOLOGY, vol. 37, no. 2-3, January 2002 (2002-01), pages 349-357, XP002312292 ISSN: 0531-5565 the whole document	1-3, 17-31
X	WO 03/000861 A (LEHRER-GRAIWER JOSH ; APFELD JAVIER (US); DILLIN ANDREW (US); GARIGAN) 3 January 2003 (2003-01-03) Methods to identify lifespan associated genes; gene therapy involving said genes the whole document	1-3, 17-31
X	US 6 025 194 A (FUNK WALTER) 15 February 2000 (2000-02-15) GC6 gene as cell senescence marker gene the whole document	1-3, 17-31

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/021944

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZHOU YIHUA ET AL: "A mammalian model for Laron syndrome produced by targeted disruption of the mouse growth hormone receptor/binding protein gene (the Laron mouse)" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 94, no. 24, 25 November 1997 (1997-11-25), pages 13215-13220, XP002312293 *ISSN: 0027-8424* The Laron or GHR/BP-deficient mouse is proposed as a useful animal model in the study of senescence page 13220 -----	1-3, 17-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/021944

Box 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. [X] Claims Nos.: 4-16 (all completely), 17-31 (all partially)
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

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 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:

see additional 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. [X] 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.:

1-30 (all partially), 31 (completely)

Remark on Protest

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

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-30 (all partially), 31 (completely)

   Invention 1: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-11

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2. claims: 1-30 (all partially), 32 (completely)

   Invention 2: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-29

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3. claims: 1-30 (all partially), 33 (completely)

   Invention 3: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-97

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4. claims: 1-30 (all partially), 34 (completely)

   Invention 4: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 4-130

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5. claims: 1-30 (all partially), 35 (completely)

   Invention 5: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-105

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6. claims: 1-30 (all partially), 36 (completely)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 6: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-38

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7. claims: 1-30 (all partially), 37 (completely)

Invention 7: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-41

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8. claims: 1-30 (all partially), 38 (completely)

Invention 8: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-43

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9. claims: 1-30 (all partially), 39 (completely)

Invention 9: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-61

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10. claims: 1-30 (all partially), 40 (completely)

Invention 10: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-9

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11. claims: 1-30 (all partially), 41 (completely)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 11: methods of determining a biological age, or rate of biological aging, or reducing a rate of biological aging, and/or delying the time of onset, or reducing the severity, of an undesirable age-related phenotype, and/or protecting against an age-related disease in a human subject, using clone 5-138

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter[redacted]nal Application No
PCT/US2004/021944

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03000861 A	03-01-2003	CA 2451247 A1	03-01-2003
		EP 1406489 A2	14-04-2004
		WO 03000861 A2	03-01-2003
		US 2003190312 A1	09-10-2003
US 6025194 A	15-02-2000	AU 1701599 A	07-06-1999
		WO 9925878 A2	27-05-1999