

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 February 2009 (05.02.2009)

PCT

(10) International Publication Number
WO 2009/018492 A3

(51) International Patent Classification:

A61K 31/7105 (2006.01) A61K 48/00 (2006.01)
A61P 9/10 (2006.01) A61P 9/00 (2006.01)

(21) International Application Number:

PCT/US2008/071837

(22) International Filing Date:

31 July 2008 (31.07.2008)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/952,911 31 July 2007 (31.07.2007) US
60/980,113 15 October 2007 (15.10.2007) US
60/980,314 16 October 2007 (16.10.2007) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
 - with sequence listing part of description (Rule 5.2(a))
- (88) Date of publication of the international search report:
21 January 2010

(54) Title: MICRO-RNAS THAT CONTROL MYOSIN EXPRESSION AND MYOFIBER IDENTITY

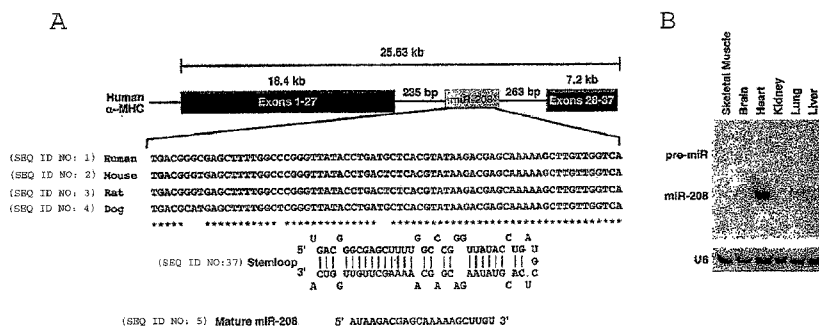


FIG. 1

(57) Abstract: The present invention relates to the identification of two microRNAs, miR-499 and miR-208b, that repress fast skeletal muscle contractile protein genes. Expression of miR-499 and/or miR-208b can be used to repress fast fiber genes and activate slow fiber genes in the treatment of musculoskeletal disorders. Inhibition of miR-499 and/or miR-208b is proposed as a treatment for cardiac hypertrophy, myocardial infarction, and/or heart failure. Pharmaceutical compositions comprising antagonists and agonists of miR-499 and miR-208b function are also disclosed.

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A. CLASSIFICATION OF SUBJECT MATTER*A61K 31/7105(2006.01)i, A61P 9/10(2006.01)i, A61K 48/00(2006.01)i, A61P 9/00(2006.01)i*

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 A61K 31/7105, A61P 9/10, A61K 48/00, A61P 9/00

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)

CA, PubMed, Delphion "(miRNA-499 OR miR-499 OR miRNA-208b OR miR-208b) OR ((MiroRNAs) AND (cardiac* OR hypertro* OR musculoskeletal))"

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHENG, Y. et al. "MicroRNAs Are Aberrantly Expressed in Hypertrophic Heart." Am. J. Pathol. Jun. 2007, Vol.170, No.6, Pages 1831-1840. See the whole document.	29-37, 54-83
A	SAYED, D. et al. "MicroRNAs Play and Essential role in the Development of Cardiac Hypertrophy." Circ. Res. Feb. 2007, Vol.100, No.3, Pages 416-424. See the whole document.	29-37, 54-83
A	THUM, T. et al. "MicroRNAs in the Human Heart. A Clue to Fetal Gene Reprogramming in Heart Failure." Circulation. 17 Jul. 2007, Vol.116, No.3, Pages 258-267. See the whole document.	29-37, 54-83
A	TATSUGUCHI, M. et al. "Expression of MicroRNAs Is Dynamically Regulated During Cardiomyocyte Hypertrophy." J. Mol. Cell. Cardiol. 14 Apr. 2007, Vol.42, No.6, Pages 1137-1141. See the whole document.	29-37, 54-83

 Further documents are listed in the continuation of Box C. See patent family 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 application or patent 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 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

27 NOVEMBER 2009 (27.11.2009)

Date of mailing of the international search report

27 NOVEMBER 2009 (27.11.2009)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

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Telephone No. 82-42-481-5634



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2008/071837

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of :

a. type of material

- a sequence listing
- table(s) related to the sequence listing

b. format of material

- on paper
- in electronic form

c. time of filing/furnishing

- contained in the international application as filed
- filed together with the international application in electronic form
- furnished subsequently to this Authority for the purposes of search

2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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.: 1-28, 38-53
because they relate to subject matter not required to be searched by this Authority, namely:
The subject matter of claims 1-28, 38-53 pertains to methods for treating or preventing the human diseases, thus relates to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT to search.
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 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.:

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.