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(72) Inventors; and

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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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

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(88) Date of publication of the international search report:
15 November 2012

(15) Information about Correction:

Previous Correction:
see Notice of 12 July 2012



WO 2012/052872 A3

(54) Title: METHODS AND COMPOSITIONS FOR THE TREATMENT OF INSULIN-ASSOCIATED MEDICAL CONDITIONS

(57) Abstract: A method of increasing insulin content in a pancreatic beta cell is disclosed. The method comprising expressing in the pancreatic beta cell an exogenous polynucleotide encoding at least one microRNA or a precursor thereof, wherein the microRNA is selected from the group consisting of miR-15, miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 and Let-7, thereby increasing the insulin content in the pancreatic beta cell.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER INV. A61K48/00 C12N5/10 ADD.				
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) A61K C12N				
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) EPO-Internal, BIOSIS, EMBASE, WPI Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	TANG XIAOQING ET AL: "Identification of glucose-regulated miRNAs from pancreatic beta cells reveals a role for miR-30d in insulin transcription", RNA, COLD SPRING HARBOR LABORATORY PRESS, US, vol. 15, no. 2, 1 February 2009 (2009-02-01), pages 287-293, XP002598119, ISSN: 1355-8382, DOI: 10.1261/RNA.1211209	6,8-10		
A	the whole document ----- -/--	1-5,7, 11-16		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.				
* Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> "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 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 </td> <td style="width: 50%; border: none; vertical-align: top;"> "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 </td> </tr> </table>			"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 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
"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 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			
23 August 2012	31/08/2012			
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Chavanne, Franz			

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2011/054446

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 2009/067644 A1 (UNIV MIAMI [US]; PASTORI RICARDO [US]; BRAVO-EGANA VALIA [US]; ROSERO) 28 May 2009 (2009-05-28) abstract paragraphs [0005], [0009], [0013], [0017], [0023], [0036] - [0038], [0048] example 3 claims 16-20	6,8-10 1-5,7, 11-16
X A	----- PANDEY A K ET AL: "MicroRNAs in diabetes: Tiny players in big disease", CELLULAR PHYSIOLOGY AND BIOCHEMISTRY 2009 S. KARGER AG CHE LNKD- DOI:10.1159/000218169, vol. 23, no. 4-6, 2009, pages 221-232, XP009156027, ISSN: 1015-8987 abstract page 222, column 2, paragraph 3 - page 225, column 1, paragraph 1	6,8-10 1-5,7, 11-16
X A	----- US 2009/291907 A1 (ESAU CHRISTINE [US] ET AL) 26 November 2009 (2009-11-26) abstract examples 27-30	6,8-10 1-5,7, 11-16
X,P	----- MELKMAN-ZEHA VI TAL ET AL: "miRNAs control insulin content in pancreatic beta-cells via downregulation of transcriptional repressors", EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 30, no. 5, March 2011 (2011-03), pages 835-845, XP055017780, ISSN: 0261-4189 the whole document	1-16
X,P	----- TATTIKOTA SUDHIR GOPAL ET AL: "Re-dicing the pancreatic beta-cell: do microRNAs define cellular identity?", EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 30, no. 5, March 2011 (2011-03), pages 797-799, XP009162202, ISSN: 0261-4189 the whole document -----	1-16

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2011/054446
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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2009067644	A1	28-05-2009	NONE	

US 2009291907	A1	26-11-2009	CA 2533701 A1	17-02-2005
			EP 1648914 A2	26-04-2006
			US 2005261218 A1	24-11-2005
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			US 2009286969 A1	19-11-2009
			US 2009291906 A1	26-11-2009
			US 2009291907 A1	26-11-2009
			US 2009298174 A1	03-12-2009
			US 2009317907 A1	24-12-2009
			US 2010249215 A1	30-09-2010
			US 2010267813 A1	21-10-2010
			US 2011224277 A1	15-09-2011
			US 2012122216 A1	17-05-2012
			US 2012157514 A1	21-06-2012
			WO 2005013901 A2	17-02-2005

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-16(partially)

Method of increasing an insulin content in a pancreatic beta cell comprising expressing an exogenous polynucleotide encoding the microRNA miR-15 in said cell, method of treating a condition associated with an insulin deficiency in a subject by administration an exogenous polynucleotide encoding the microRNA miR-15, polynucleotide encoding the microRNA miR-15 for treating a condition associated with an insulin deficiency, nucleic acid construct comprising a nucleic acid sequence encoding the microRNA miR-15 operably linked to a pancreatic beta cell promoter, pharmaceutical composition comprising said nucleic acid construct, isolated pancreatic beta cell comprising said construct, said cell for the treatment of diabetes, method of decreasing an insulin content in a pancreatic beta cell by administration of an agent downregulating expression of miR-15, treatment method based on the downregulation of miR-15.

2-14. claims: 1-16(partially)

Method of increasing an insulin content in a pancreatic beta cell comprising expressing an exogenous polynucleotide encoding the microRNA miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively, in said cell, method of treating a condition associated with an insulin deficiency in a subject by administration an exogenous polynucleotide encoding the microRNA miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively, polynucleotide encoding the microRNA miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively, for treating a condition associated with an insulin deficiency, nucleic acid construct comprising a nucleic acid sequence encoding the microRNA miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively, operably linked to a pancreatic beta cell promoter, pharmaceutical composition comprising said nucleic acid construct, isolated pancreatic beta cell comprising said construct, said cell for the treatment of diabetes, method of decreasing an insulin content in a pancreatic beta cell by administration of an agent downregulating expression of miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively, treatment method based on the downregulation of miR-16, miR-24, miR-26, miR-27, miR-29, miR-30, miR-129, miR-141, miR-148, miR-182, miR-200, miR-376 or Let-7, respectively.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. (means)
 on paper
 in electronic form
 - b. (time)
 in the international application as filed
 together with the international application in electronic form
 subsequently to this Authority for the purpose 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:

INTERNATIONAL SEARCH REPORT

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PCT/IB2011/054446

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.:
because they relate to subject matter not required to be searched by this Authority, namely:

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:

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 fees, this Authority did not invite payment of additional fees.
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.:

1-16(partially)
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.