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(71) **Applicant** *(for all designated States except US)*: **GEN9, INC.** [US/US]; 500 Technology Square, Suite 130, Cambridge, Massachusetts 02139 (US).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **JACOBSON, Joseph** [US/US]; 223 Grant Avenue, Newton, Massachusetts 02459 (US). **KUNG, Li-yun, A.** [US/US]; 4 Knowles Farm Road, Arlington, MA 02474 (US). **WILSON, Andrew, Kirk** [US/US]; 4 Gay Street, Arlington, MA 02474 (US). **RAMU, Senthil** [IN/US]; 6 Whittier Place #5J, Boston, MA 02114 (US). **SCHINDLER, Daniel** [US/US]; 31 Williams Street, Newton, MA 02464 (US). **HUDSON, Mike** [CA/US]; 21 Crestwood Drive, Framingham, MA 01701 (US).

(74) **Agent**: **CAMACHO, Jennifer, A.**; Greenberg Traurig, One International Place, Boston, MA 02061 (US).

(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, CL, 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, 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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[Continued on next page]

(54) **Title**: METHODS AND DEVICES FOR NUCLEIC ACIDS SYNTHESIS

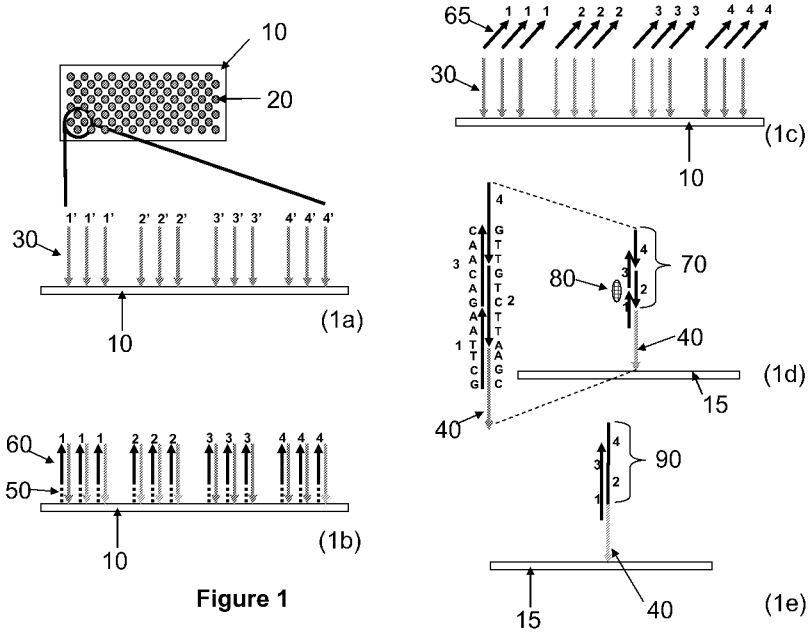

Figure 1

(57) **Abstract**: Methods and apparatus relate to the synthesis of polynucleotides having a predefined sequence on a support. Assembly methods include primer extension to generate overlapping construction oligonucleotides and assembly of the polynucleotides of interest onto an anchor support-bound oligonucleotides. Methods and apparatus for selection of polynucleotides having the predefined sequence and/or length are disclosed.

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DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/10 C12N15/66 C12P19/34
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)
C12N C12P

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, CAB Data, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2004/024886 A2 (COMBIMATRIX CORP [US]) 25 March 2004 (2004-03-25) the whole document	1-20, 32-65
A	WO 2005/059096 A2 (MASSACHUSETTS INST TECHNOLOGY [US]; CARR PETER A [US]; CHOW BRIAN Y [U) 30 June 2005 (2005-06-30) the whole document	1-20, 32-65
A	WO 2010/025310 A2 (WESTEND ASSET CLEARINGHOUSE CO [US]; JACOBSON JOSEPH [US]; CHURCH GEOR) 4 March 2010 (2010-03-04) the whole document	1-20, 32-65

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

[X] 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

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"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

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"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
19 March 2012	09/07/2012

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, Fax: (+31-70) 340-3016	Hornig, Horst

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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.
X,P	WO 2011/085075 A2 (GEN9 INC [US]; JACOBSON JOSEPH [US]; CHU LARRY LI-YANG [US]) 14 July 2011 (2011-07-14) page 53, paragraph [0092] - page 53, paragraph [0093]; figures 9A,9B,10A,10B	1-20,42, 45-48
A	DE 43 43 591 A1 (EVOTEC BIOSYSTEMS GMBH [DE]) 22 June 1995 (1995-06-22) the whole document	1-20, 32-65
A	WO 01/88173 A2 (HERCULES INC [US]) 22 November 2001 (2001-11-22) the whole document	1-20, 32-65
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A	WO 99/14318 A1 (UNIV TEXAS [US]; EVANS GLEN A [US]) 25 March 1999 (1999-03-25) the whole document	1-20, 32-65

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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.
A	WO 2007/010252 A1 (SOLEXA LTD [GB]; SMITH GEOFFREY PAUL [GB]) 25 January 2007 (2007-01-25) figure 1	42
A	WO 2008/041002 A2 (SOLEXA LTD [GB]; RIGATTI ROBERTO [GB]; OST TOBIAS [GB]; FASHENA SARAH) 10 April 2008 (2008-04-10) figures 1-4	42

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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.:

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.:

1-20, 32-65

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-20, 32-65

Method for producing polynucleotides: a) providing a first and second plurality of support-bound single-stranded oligos, each first plurality of oligo comprises a 3' region that is complementary to the 3' region of the second plurality of oligos; b) generating a first and second plurality of construction oligos complementary to first and second support-bound oligos in a chain extension reaction; c) providing a plurality support-bound anchor single-stranded oligos at a selected feature, wherein 5' end of the plurality of the first anchor oligo is the same as a sequence region of the first plurality of support bound oligos; d) hybridizing first and second plurality of construction oligos to the plurality of anchor oligos; and e) ligating the first and second plurality of construction oligos, thereby generating the at least one polynucleotide; a method of synthesizing a polynucleotide having a predefined sequence comprising the steps a) to d) as defined in claim 32; a nucleic acid array comprising the features a. to c. as defined in claim 42; a method of producing a plurality of polynucleotides having a predefined sequence comprising the steps a) to g) as defined in claim 45; a method for synthesizing a plurality of polynucleotide having a predefined sequence comprising the steps a) to f) as defined in claim 49.

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2. claims: 21-31

Method for generating a polynucleotide havinbg a predefined sequence, the method comprising: a) synthesizing a plurality of support-bound double-stranded polynucleotides comprising a free single-stranded overhang, the plurality of polynucleotide sequences comprising the predefined polynucleotide sequence, wherein single-stranded overhang comprises the sequence of a terminal construction oligonucleotide N; b) providing a stem-loop oligonucleotide comprising a single-stranded overhang wherein the single-stranded overhang is complementary to the terminal construction oligonucleotidesequence N; c) hybridizing the stem-loop oligonucleotide to the free overhang of the polynucleotide having predefined sequences; d) ligating the stem-loop oligonucleotide to the free overhang of the polynucleotide having predefined sequence; and e) degrading polynucleotide sequences that do not comprise the terminal construction oligonucleotide sequence N.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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