



- (51) International Patent Classification:
C12Q 1/68 (2006.01)
- (21) International Application Number:
PCT/US2014/033814
- (22) International Filing Date:
11 April 2014 (11.04.2014)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/853,758 11 April 2013 (11.04.2013) 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, BN, 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, IR, IS, JP, KE, KG, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
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.
- (84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, 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,

[Continued on next page]

- (54) Title: TEMPLATE-DIRECTED
- γ
- PNA SYNTHESIS AND
- γ
- PNA TARGETING COMPOUNDS

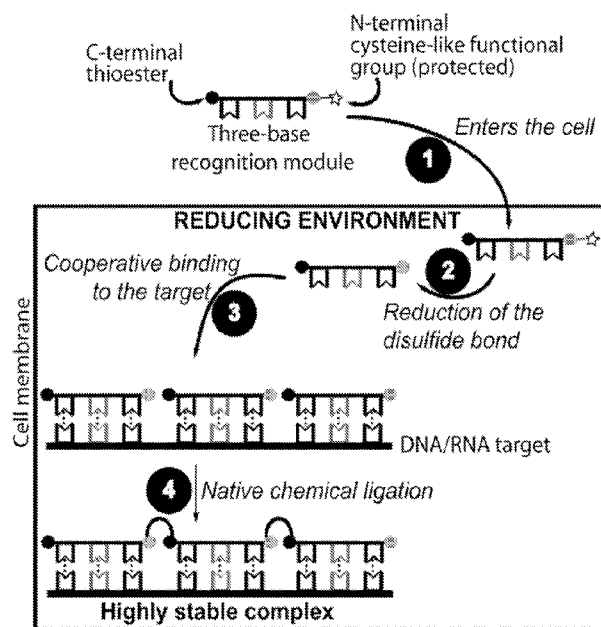


Fig. 1

(57) Abstract: Described herein are recognition modules that bind specifically to a template nucleic acid and which ligate together in a reducing environment to produce a gamma peptide nucleic acid (γ PNA) oligomer. Also provided are methods of synthesizing a γ PNA oligomer on a template using the recognition modules.



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

— with sequence listing part of description (Rule 5.2(a))

Published:

(88) Date of publication of the international search report:

12 February 2015

— with international search report (Art. 21(3))

INTERNATIONAL SEARCH REPORT

2014/033814 23.11.2014

International application No.

PCT/US2014/033814

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12Q 1/68 (2014.01)

USPC - 435/6.1

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)

IPC(8) - C07H 21/00; C07K 1/00; C12Q 1/68 (2014.01)

USPC - 435/6.1; 530/324, 350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61K 38/00; C12Q 1/6883, 2600/156, 2600/158 (2014.09) (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, STN, Google Patents, Google Scholar, Google.

Search terms used: PNA peptide nucleic acid nucleobase oligomer pteridin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/0009041 A1 (BUCHARDT et al) 13 January 2005 (13.01.2005) entire document	1-13, 15, 18-20, 24-29, 31, 37-40
A	WO 2004/024757 A2 (RASMUSSEN et al) 25 March 2004 (25.03.2004) entire document	1-13, 15, 18-20, 24-29, 31, 37-40
A	WO 2012/138955 A2 (LY et al) 11 October 2012 (11.10.2012) entire document	1-13, 15, 18-20, 24-29, 31, 37-40
A	US 6,355,726 B1 (DOEMLING et al) 12 March 2002 (12.03.2002) entire document	1-13, 15, 18-20, 24-29, 31, 37-40

☐ Further documents are listed in the continuation of Box C.

* 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 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

23 October 2014

Date of mailing of the international search report

25 NOV 2014

Name and mailing address of the ISA/US

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PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

014/033814-25-11-2014
International application No.

PCT/US2014/033814

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:

Claims 1-13, 15, 18-20, 24-29, 31, and 37-40 have been analyzed subject to the restriction that the claims read on the Formula 1 as described in the Lack of Unity of Invention (See Extra Sheet). The claims are restricted to a method of producing gamma-PNA oligomers, comprising contacting a template nucleic acid in a reducing environment, with a plurality of recognition modules of Formula 1: in which X is S; n is 1; m is 0; R1 is each independently H; R2 is H; R3 is (C1-C10) divalent hydrocarbon; R4 is OH; R for each of the plurality of recognition modules each independently are nucleobases producing a sequence of nucleobases complementary to a target sequence of nucleobases in the template nucleic acid so that each of the plurality of recognition modules bind to the target sequence of nucleobases on the template nucleic acid and ligate to each other; where each R is each JB1; a composition having the structure of Formula 1; a composition comprising the compound and a transfection reagent; and a kit comprising a composition in a vessel.

See Extra 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 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.:
1-13, 15, 18-20, 24-29, 31, 37-40

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.

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. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: Claims 1-40 are drawn to a method of producing gamma-PNA oligomers, comprising contacting a template nucleic acid in a reducing environment, with a plurality of recognition modules of Formula 1, a composition having the structure of Formula 1, a composition comprising the compound and a transfection reagent, and a kit comprising a composition in a vessel.

The first invention of Group I+ is restricted to a method of producing gamma-PNA oligomers, comprising contacting a template nucleic acid in a reducing environment, with a plurality of recognition modules of Formula 1: in which X is S; n is 1; m is 0; R1 is each independently H; R2 is H; R3 is (C1-C10) divalent hydrocarbon; R4 is OH; R for each of the plurality of recognition modules each independently are nucleobases producing a sequence of nucleobases complementary to a target sequence of nucleobases in the template nucleic acid so that each of the plurality of recognition modules bind to the target sequence of nucleobases on the template nucleic acid and ligate to each other; where each R is each JB1; a composition having the structure of Formula 1; a composition comprising the compound and a transfection reagent; and a kit comprising a composition in a vessel. It is believed that claims 1-13, 15, 18-20, 24-29, 31, 37-40 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

Applicant is invited to elect additional formula(e) for each additional compound to be searched in a specific combination by paying an additional fee for each set of election. An exemplary election would be a method of producing gamma-PNA oligomers, comprising contacting a template nucleic acid in a reducing environment, with a plurality of recognition modules of Formula 1: in which X is O; n is 1; m is 0; R1 is each independently H; R2 is H; R3 is (C1-C10) divalent hydrocarbon; R4 is OH; R for each of the plurality of recognition modules each independently are nucleobases producing a sequence of nucleobases complementary to a target sequence of nucleobases in the template nucleic acid so that each of the plurality of recognition modules bind to the target sequence of nucleobases on the template nucleic acid and ligate to each other; where each R is each JB1; a composition having the structure of Formula 1; a composition comprising the compound and a transfection reagent; and a kit comprising a composition in a vessel. Additional formula(e) will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ 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 Groups I+ formulae do not share a significant structural element, requiring the selection of alternatives for the compound variables X, n, m, R1, R2, R3, R4, and R.

The Groups I+ share the technical features of a method of producing gamma-PNA oligomers, comprising contacting a template nucleic acid in a reducing environment, with a plurality of recognition modules having the core structure of Formula 1, a composition having the core structure of Formula 1, a composition comprising the compound and a transfection reagent, and a kit comprising a composition in a vessel. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2005/0009041 A1 to Buchardt et al. teach a method of producing gamma-PNA oligomers (Para. [0104], PNA oligomers of the invention can be synthesized with the G group in either orientation.), comprising contacting a template nucleic acid in a reducing environment (Paras. [0354] through [0355], preparation of PNA backbone by reductive amination; Para. [0356], the coupling reaction occurs using palladium on carbon as the reducing agent), with a plurality of recognition modules having the core structure of Formula 1 of the instant case (Para. [0050], Preferred peptide nucleic acids have general formula (III), ...see shown structure...; Fig. 1(B)), a composition having the core structure of Formula 1 (Para. [0159], For therapeutic or prophylactic treatment, the peptide nucleic acids of the invention can be formulated in a pharmaceutical composition...; Para. [0050], Preferred peptide nucleic acids have general formula (III), ...see shown structure...), and a kit comprising a composition in a vessel (Para. [0160], The pharmaceutical composition may be administered in a number of ways depending on whether local or systemic treatment is desired, and on the area to be treated.; Para. [0162], Compositions for oral administration include powders or granules, suspensions or solutions in water or non-aqueous media, capsules, sachets, or tablets.).

Specifically, WO 2004/024757 A2 to Rasmussen et al. teach a composition having the core structure of Formula 1 (Pg. 60, Pns. 12-15, Then a peptide nucleic acid molecule of the invention is synthesized according to scheme 2:...; Pg. 61, Scheme 2, ...see final compound of scheme 2, wherein B is a naturally-occurring nucleobase; ...see shown structure...) a composition comprising the compound and a transfection reagent (Pg. 80, Lns: 24-33, The PNAs were evaluated in vitro using BNL CL2 mouse liver cell line, PNA intracellular delivery was achieved by annealing the PNA to a partly complementary DNA-oligo followed by co-transfection using polyethylenimine transfection reagent.).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.