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— *with international search report*

[Continued on next page]

(54) Title: SELECTION OF NUCLEIC ACID-BASED SENSOR DOMAINS WITHIN NUCLEIC ACID SWITCH PLATFORM

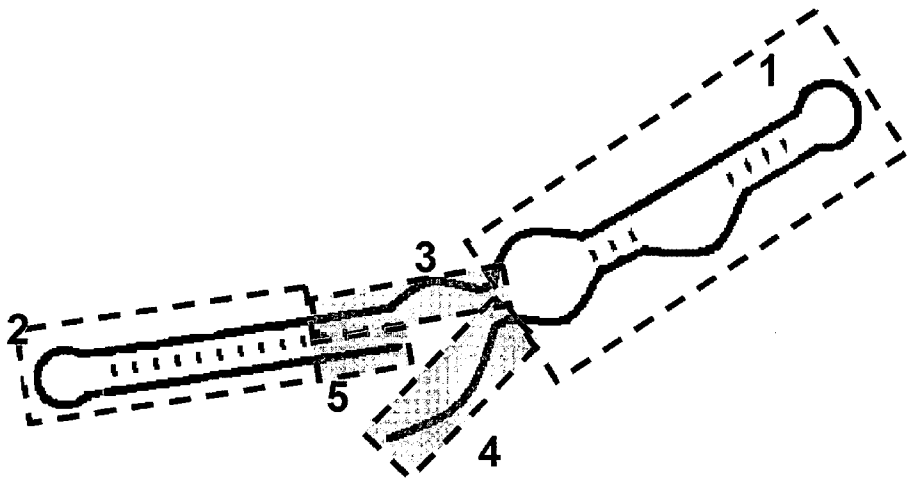

Figure 1

(57) Abstract: The invention relates to a method (preferably a high throughput method) for screening for functional aptamer-regulated, ligand-responsive nucleic acids, or 'ampliSwitches,' and uses thereof. The subject method not only applies to large molecules, such as proteins, but also applies to relatively small ligands, such as those with molecular weight of no more than 5 kDa, 3 kDa, or 1 kDa.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/11 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)
C12Q 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 practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/086669 A (CALIFORNIA INST OF TECHN [US]; SMOLKE CHRISTINA D [US]; BAYER TRAVIS S) 17 August 2006 (2006-08-17) page 3, paragraph 1; figures 1A,1B,5,9 page 10, paragraph 3 - page 13, paragraph 1	1-45, 47-55
X	SMOLKE, C.: "Molecular Switches for Cellular Sensors" ENGINEERING & SCIENCE, [Online] vol. 67, no. 4, 2005, pages 28-37, XP002514464 Retrieved from the Internet: URL:http://eands.caltech.edu/articles/LXVI I4/Smolke%20Feature%20in%20Spreads.pdf> [retrieved on 2009-02-05] page 36, column 2, paragraph 2 - page 37, column 2, paragraph 1	1-45, 47-55

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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 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

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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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"&" 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 February 2009	26/05/2009

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/008659

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BUSKIRK ET AL: "Engineering a ligand-dependent RNA transcriptional activator" CHEMISTRY AND BIOLOGY, CURRENT BIOLOGY, LONDON, GB, vol. 11, 1 August 2004 (2004-08-01), pages 1157-1163, XP002985924 ISSN: 1074-5521 the whole document	1-45, 47-55
X	DESAI S K ET AL: "Genetic screens and selections for small molecules based on a synthetic riboswitch that activates protein translation" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC.; US, US, vol. 126, 1 January 2004 (2004-01-01), pages 13,247-13,254, XP002982412 ISSN: 0002-7863 the whole document	1-45, 47-55
X	SUDARSAN NARASIMHAN ET AL: "Tandem riboswitch architectures exhibit complex gene control functions." SCIENCE (NEW YORK, N.Y.) 13 OCT 2006, vol. 314, no. 5797, 13 October 2006 (2006-10-13), pages 300-304, XP002514465 ISSN: 1095-9203 page 302, column 2, paragraph 2 - paragraph 3; figure 2 page 304, column 1, paragraph 2	1,3-6,9, 12,14, 19,35, 36,44, 45, 47-49, 53-55
A	AN CHUNG-IL ET AL: "Artificial control of gene expression in mammalian cells by modulating RNA interference through aptamer-small molecule interaction." RNA (NEW YORK, N.Y.) MAY 2006, vol. 12, no. 5, May 2006 (2006-05), pages 710-716, XP002514466 ISSN: 1355-8382 abstract; figures 1-4	1-45, 47-55
A	US 2006/088864 A1 (SMOLKE CHRISTINA D [US] ET AL) 27 April 2006 (2006-04-27) paragraph [0020] - paragraph [0029] paragraph [0033] paragraph [0087] paragraph [0098] paragraph [0104] - paragraph [0106] paragraph [0184] - paragraph [0201]; figure 2	1-45, 47-55

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/008659

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BAYER TRAVIS S ET AL: "Programmable ligand-controlled riboregulators of eukaryotic gene expression" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 23, no. 3, 1 March 2005 (2005-03-01), pages 337-343, XP002456695 ISSN: 1087-0156 page 337, column 2, paragraph 2; figures 1a-b	1-45, 47-55
A	SUESS BEATRIX ET AL: "A theophylline responsive riboswitch based on helix slipping controls gene expression in vivo." NUCLEIC ACIDS RESEARCH 2004, vol. 32, no. 4, 2004, pages 1610-1614, XP002514467 ISSN: 1362-4962 abstract; figure 1 page 1611, column 1, paragraph 2	1,2, 4-45, 47-55
A	US 2002/150996 A1 (NILSEN-HAMILTON MARIT [US]) 17 October 2002 (2002-10-17) paragraph [0043] - paragraph [0045]; figures 2,3 paragraph [0050] - paragraph [0051]	1-45, 47-55
A	DAVIDSON ERIC A ET AL: "Synthetic RNA circuits" NATURE CHEMICAL BIOLOGY, vol. 3, no. 1, January 2007 (2007-01), pages 23-28, XP002514468 ISSN: 1552-4450(print) 1552-4469(ele page 24, column 1, paragraph 2 - column 2, paragraph 2; figure 1 page 26, column 2, paragraph 2 - paragraph 3	1-45, 47-55
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A	ISAACS F J ET AL: "RNA synthetic biology" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 24, no. 5, 5 May 2006 (2006-05-05), pages 545-554, XP002456699 ISSN: 1087-0156 the whole document	1-45, 47-55

INTERNATIONAL SEARCH REPORT

International application No.
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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 allsearchable 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 reportcovers 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.:

see additional sheet(s)

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: 1-45, 47-55 (in part)

Method of screening a library of nucleic acids, wherein each member comprises (a) an aptamer that potentially binds a ligand and (b) a functional domain; comprising steps of (1) contacting the library with the ligand, (2) isolating those nucleic acids that bind, and (3) determining whether ligand binding to (a) favors a conformational change in (b); wherein said functional domain (b) is not a ribozyme or a catalytic RNA.

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2. claims: 1-55 (in part)

Method of screening a library of nucleic acids, wherein each member comprises (a) an aptamer that potentially binds a ligand and (b) a functional domain; comprising steps of (1) contacting the library with the ligand, (2) isolating those nucleic acids that bind, and (3) determining whether ligand binding to (a) favors a conformational change in (b); wherein step (2) is not effectuated by denaturing PAGE or a chromatography-based selection system.

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3. claims: 1-55 (in part)

Method of screening a library of nucleic acids, wherein each member comprises (a) an aptamer that potentially binds a ligand and (b) a functional domain; comprising steps of (1) contacting the library with the ligand, (2) isolating those nucleic acids that bind, and (3) determining whether ligand binding to (a) favors a conformational change in (b); wherein said functional domain (b) is not a ribozyme or a catalytic RNA, and wherein step (2) is not effectuated by denaturing PAGE or a chromatography-based selection system.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/008659

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006086669 A	17-08-2006	NONE	
US 2006088864 A1	27-04-2006	EP 1799825 A2	27-06-2007
		JP 2008515405 T	15-05-2008
		WO 2006042112 A2	20-04-2006
US 2002150996 A1	17-10-2002	NONE	