

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
17 January 2002 (17.01.2002)

PCT

(10) International Publication Number
WO 02/004681 A3

- (51) International Patent Classification⁷: **C12Q 1/68**, G01N 1/30
- (21) International Application Number: PCT/US01/21846
- (22) International Filing Date: 11 July 2001 (11.07.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/217,782 11 July 2000 (11.07.2000) US
- (71) Applicant: **NORTHWESTERN UNIVERSITY**
[US/US]; 633 Clark Street, Evanston, IL 60208 (US).
- (72) Inventors: **LETSINGER, Robert, L.**; 316 Third Street, Wilmette, IL 60091 (US). **GARIMELLA, Viswanadham**; 1915 Maple Avenue, Englehart Hall, Apt. 323, Evanston, IL 60201 (US).
- (74) Agent: **MIAO, Emily**; McDonnell Boehnen Hulbert & Berghoff, 300 South Wacker Drive, Suite 3200, Chicago, IL 60606 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
- (88) Date of publication of the international search report:
7 August 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 02/004681 A3

(54) Title: METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING

(57) Abstract: The present invention relates to a method for amplifying a detection signal by enhancing or promoting the deposition of additional silver in assay detection systems where the formation of a silver spot serves as a reporter for the presence of a target molecule, including biological polymers (e.g., proteins and nucleic acids) and small molecules.

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 01/21846A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 G01N1/30

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 7 C12Q

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, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HACKER G W: "HIGH PERFORMANCE NANOGOLD-SILVER IN SITU HYBRIDISATION" EUROPEAN JOURNAL OF HISTOCHEMISTRY, XX, XX, vol. 42, 1998, pages 111-120, XP009003539 cited in the application the whole document ---	1-30
A	LETSINGER R L ET AL: "Use of a steroid cyclic disulfide anchor in constructing gold nanoparticle- oligonucleotide conjugates" BIOCONJUGATE CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 11, no. 2, March 2000 (2000-03), pages 289-291, XP002205939 ISSN: 1043-1802 the whole document --- -/--	1-30

 Further documents are listed in the continuation of box C. Patent family members are listed in 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

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

24 January 2003

Date of mailing of the international search report

04/02/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Moreno de Vega, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/21846

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	BENDAYAN MOISE: "A review of the potential and versatility of colloidal gold cytochemical labeling for molecular morphology." BIOTECHNIC & HISTOCHEMISTRY, vol. 75, no. 5, September 2000 (2000-09), pages 203-242, XP001121888 ISSN: 1052-0295 the whole document -----	1-30
P,A	TATON T ANDREW ET AL: "Scanometric DNA array detection with nanoparticle probes." SCIENCE (WASHINGTON D C), vol. 289, no. 5485, 2000, pages 1757-1760, XP002158394 ISSN: 0036-8075 abstract -----	1-30