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Published:

- with international search report
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16 October 2008

(54) Title: NANOPLASMONIC MOLECULAR RULER FOR NUCLEASE ACTIVITY AND DNA FOOTPRINTING

(57) Abstract: This invention provides a nanoplasmic molecular ruler, which can perform label-free and real-time monitoring of nucleic acid (e.g., DNA) length changes and perform nucleic acid footprinting. In various embodiments the ruler comprises a nucleic acid attached to a nanoparticle, such that changes in the nucleic acid length are detectable using surface plasmon resonance. The nanoplasmic ruler provides a fast and convenient platform for mapping nucleic acid-protein interactions, for nuclease activity monitoring, and for other footprinting related methods.



INTERNATIONAL SEARCH REPORT

International application No

PCT/US07/20026

A CLASSIFICATION OF SUBJECT MATTER
 IPC C07H 21/00(2006 01),21/02(2006 01),C12Q 1/68(2006 01)

 USPC 536/23 1,977/773
 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)
 U S 536/23 1, 977/773

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)
 Please See Continuation Sheet

C DOCUMENTS CONSIDERED TO BE RELEVANT

Category ♦	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X,P	US 7,250,499 B2 (MIRKIN et al) 31 July 2007 (31 07 2007), see entire document, particularly claims 1-18	52, 53, 55, 59-61, 66
X	SONNICHSEN et al "A molecular ruler based on plasmon coupling of single gold and silver nanoparticles" Nature Biotechnology June 2005, Vol 23, No 6, pages 741-745, entire document	52, 53, 55, 59-61, 66

D Further documents are listed in the continuation of Box C See patent family annex

♦ Special categories of cited documents	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search 12 July 2008 (12 07 2008) Date of mailing of the international search report 07 AUG 2008

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Continuation of B. FIELDS SEARCHED Item 3:

EAST and PubMed, search terms measur*, detect*, nucleic acid length, surface plasmon resonance, nanoparticle, conjugat*, nucleic acid

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

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 must be paid.

Group I, claim(s) 1-49, 51-63, 65-68 and 94-104, drawn to a nanoplasmon resonance ruler comprising a nanoparticle having a nucleic acid attached thereto to form a nanoparticle-nucleic acid conjugate.

Group II, claim(s) 69-80 and 93, drawn to a method of identifying the presence of and/or determining the location of a binding site of a molecule that binds to a nucleic acid.

Group III, claim(s) 81-90, 93, and 105, drawn to a method of detecting a mismatch in a nucleic acid hybridization said method comprising the digestion of a double-stranded nucleic acid with a non-specific exonuclease and detecting the change in resonance resulting from the digestion.

Group IV, claim(s) 91-93, drawn to a method of detecting a mismatch in a nucleic acid hybridization said method comprising the digestion of a terminal single-stranded nucleic acid with a single-strand specific exonuclease and detecting the change in resonance resulting from said digestion.

The inventions listed as Groups I-IV 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 technical features linking the groups do not share a common structural feature. The methods of inventions III and IV use different materials in the steps of performing the method.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. The species are as follows: the composition of the nanoparticle. For example, the material selected from the group recited in claims 12 and 13, the surface functionalized material on the nanoparticle, and the chemical structure of the nucleic acid such that the restriction site is disclosed.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the species are composed of different structural elements with different functional effects.

INTERNATIONAL SEARCH REPORT

International application No

PCT/US07/20026

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 50 and 64
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
there is reference to a sequence identifier but no sequence listing is in the file history of the application

- 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
Please See Continuation 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 any 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
- Remark on Protest The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee
- D** 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