Abstract: Highly sensitive system and methods for analysis of prostate specific antigen (PSA). The invention described herein provides methods, compositions, kits, and systems for the sensitive detection of prostate specific antigen. Such methods, compositions, kits, and systems are useful in diagnosis, prognosis, and determination of methods of treatment in conditions that involve release of prostate specific antigen.
INTERNATIONAL SEARCH REPORT

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01 N 33/674 (2009.01)
USPC - 435/7,23
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)-G01 N 33/674 (2009 01)
USPC-435/7 23, 288 7, 436/164, 172, 530/388 8

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)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB),Google Patents, Google Scholar
capillary, antibody, fluorescent, femtogram, detection, prostate specific antigen, kallikrein, flow cell, single-molecule,

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>(SCHWEITZER et al.) Immunoassays with rolling circle DNA amplification A versatile platform for ultrasensitive antigen detection PNAS August 29, 2000 vol 97 no 18 101-131/01 19 (pg 10114 Fig 1), (pg 10115, para 91), (pg 10116 para 4), (pg 10116 Fig 3) (pg 10117 para 1), (pg 10118 para 2), (pg 10119 para 1)</td>
<td>1-15, 17-22, 33-39, 46</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C

| V | 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
02 February 2009 (02 02 2009)

Date of mailing of the international search report
18 FEB 2009

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No 571-273-3201

Authorized officer
PCT Helpdesk 571-272-4200
PCTOIS 571-272 7774

Form PCT/ISA/2 10 (second sheet) (April 2007)
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. I Claims Nos. because they relate to subject matter not required to be searched by this Authority, namely:

2. I 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 earned out, specifically:

3. D Claims Nos. because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 64(a):

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

The International Bureau of WIPO found multiple inventions in this international application, as follows:

1. I As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. I As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. I 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. X 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. 1-22, 33-39, and 46.

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Continuation of Box No III Lack of Unity

This application contains the following inventions or groups of inventions which are not so linked as to from 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: Claims 1-22, 33-39, and 46 are directed to either a method for detecting a single prostate specific antigen (PSA) molecule, fragment, or complex in a sample at a level less that 100 pg/ml (1-16), a method of diagnosing prostate cancer based on levels of PSA (17-20), a method for detecting a single prostate specific antigen (PSA) molecule fragment or complex in a sample at a level less than 5 pg/ml (21-22), a method for determining a diagnosis, prognosis, or method of treatment in an individual (25-39), or a composition (46).

Group II: Claims 23-24 are directed to either a method for assessing the likelihood of recurrence of cancer in an individual (23-24).

Group III: Claims 25-30 are directed to either a method of monitoring decreases in a level of PSA after surgical resection (25-26) or a method of monitoring the effectiveness of a therapeutic treatment in an individual (27-30).

Group IV: Claims 31-32 are directed to a method for screening an individual for the presence of breast cancer.

Group V: Claims 40-45 and 47-54 are directed to either a composition for the detection of a prostate specific antigen (PSA) or a kit.

The inventions listed as Groups I-V 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 special technical feature that links Groups I-V is the detection of PSA. Groups I and II are additionally linked by requiring the detection of PSA at a level less than 100 pg/ml. Groups I, II and VI are additionally linked by requiring a reagent capable of labeling PSA. Groups I and III are additionally linked by requiring detection in a series of samples from the subject. However, none of these technical features represents an improvement over the prior art of US 2002/0058291 A1 (Mikolajczyk et al.) which teaches detecting PSA at 60 pg/ml (para [0123]) and further teaches detection in a series of samples (monitoring, para [0030]) and further teaches a reagent capable of labeling PSA (labeled antibody, para [0052]). Accordingly, unity of invention is lacking under PCT Rule 13.1.