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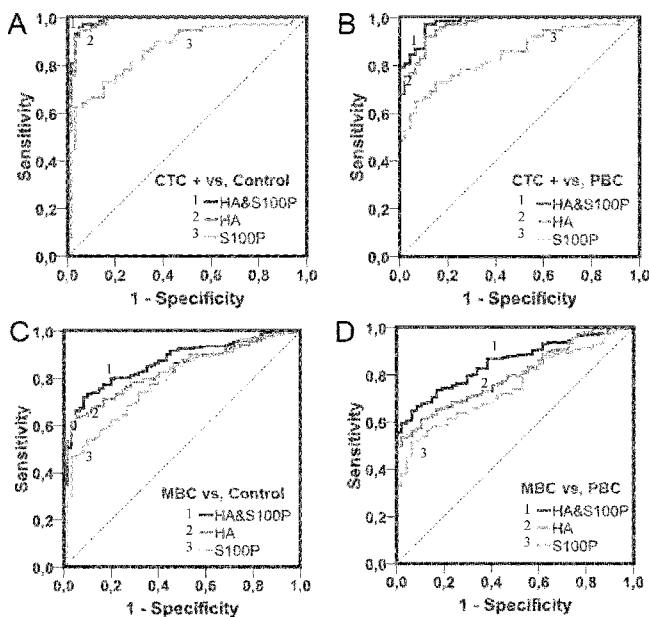
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[Continued on next page]

(54) Title: S1 OOP AND HYLURONIC ACID AS BIOMARKERS FOR METASTATIC BREAST CANCER

Figure 2:



(57) Abstract: The present invention pertains to a new method for the diagnosis, prognosis, stratification and/or monitoring of a therapy, of breast cancer in a patient. The method is based on the use of hyaluronic acid and S100P as combined biomarkers in the plasma of breast cancer patients. The new biomarkers of the invention allow diagnosing and even stratifying of breast cancer, in particular metastatic breast cancer. The method provides an interesting alternative to present procedures such as the analysis of the circulating tumor cells (CTC) status. The biomarkers of the invention furthermore allow to monitor therapy success of breast cancer patients and to estimate a patient's prognosis.



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, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,  
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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 (Rule 48.2(h))*

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INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2015/057946

A. CLASSIFICATION OF SUBJECT MATTER  
INV. G01N33/574  
ADD.  
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)  
G01N

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)  
EPO-Internal, BIOSIS, EMBASE, INSPEC, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BERTRAND DELPECH ET AL: "Serum hyaluronan (hyaluronic acid) in breast cancer patients", INTERNATIONAL JOURNAL OF CANCER, vol. 46, no. 3, 15 September 1990 (1990-09-15), pages 388-390, XP055050210, ISSN: 0020-7136, DOI: 10.1002/ijc.2910460309	1,2,4,5, 8-13,15
A	the whole document In particular: Title; Abstract; Patients and methods section. ----- -/--	3,14

Further documents are listed in the continuation of Box C.

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 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  2 June 2015	Date of mailing of the international search report  16/11/2015
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  C.F. Angioni
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2015/057946

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE LA TORRE M ET AL: "Localization of hyaluronan in normal breast tissue, radial scar, and tubular breast carcinoma", HUMAN PATHOLOGY, SAUNDERS, PHILADELPHIA, PA, US, vol. 24, no. 12, 1 December 1993 (1993-12-01), pages 1294-1297, XP026255607, ISSN: 0046-8177, DOI: 10.1016/0046-8177(93)90262-F [retrieved on 1993-12-01]	1,2,4,5, 8-13,15
A	the whole document In particular: Title; Abstract; Materials and methods section.	3,14
X	----- MARÍA D CORTE ET AL: "Expression and Clinical Signification of Cytosolic Hyaluronan Levels in Invasive Breast Cancer", BREAST CANCER RESEARCH AND TREATMENT, KLUWER ACADEMIC PUBLISHERS, BO, vol. 97, no. 3, 10 May 2006 (2006-05-10), pages 329-337, XP019392286, ISSN: 1573-7217, DOI: 10.1007/S10549-005-9130-7	1,2,4,5, 8-13,15
A	the whole document In particular: Title; Abstract; Patients and methods section. -----	3,14

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2015/057946

## 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 all searchable 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 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.:

1-5, 8-15(all partially)

### 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: 1-5, 8-15(all partially)

The methods, kits and uses as defined in claims 1-5 and 8-15, wherein the biomarker is an ECM.

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2. claims: 6, 7(completely); 1-5, 8-15(partially)

The methods, kits and uses as defined in claims 1-15, wherein the biomarker is an S100 family protein.

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