Title: NOVEL NUCLEOTIDE AND AMINO ACID SEQUENCES, AND ASSAYS AND METHODS OF USE THEREOF FOR DIAGNOSIS OF CARDIAC DISEASE

Abstract: Novel markers for cardiac disease that are both sensitive and accurate. These markers are differentially and/or specifically expressed in cardiac tissue, as opposed to other types of tissues, optionally and preferably including muscle tissue. The measurement of these markers, alone or in combination, in patient samples provides information that the diagnostician can correlate with a probable diagnosis of cardiac disease, including pathology and/or damage, including acute and/or chronic damage. The markets of the present invention, alone or in combination, reveal a high degree of differential detection between cardiac disease states and non-cardiac disease states.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
C07K14/47  G01N33/68  C07K16/18

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)
C07K  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 practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, Sequence Search

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>
</table>
| X        | BHAVSAR PANKAJ K ET AL: "Isolation and characterization of the human cardiac troponin I gene (TNNI3)"
GENOMICS,
vol. 35, no. 1, 1996, pages 11-23,
XP002350371
ISSN: 0888-7543
abstract
page 11, left-hand column, paragraph 1 -
page 12, left-hand column, last paragraph;
figures 1,2; table 1
page 19, left-hand column, last paragraph
right-hand column, paragraph 1
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/\-

Further documents are listed in the continuation of box C.

* 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

Date of the actual completion of the international search
9 February 2006

Date of mailing of the international search report
21 03 2006

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
Luis Alves, D

Form PCT/ISA/210 (second sheet) (January 2004)
<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>TOYOTA NAOJI ET AL: &quot;Thin-filament-binding domains of cardiac and fast skeletal muscle troponin I isoforms as studied by epitope tagging&quot; JOURNAL OF MUSCLE RESEARCH AND CELL MOTILITY, vol. 20, no. 8, November 1999 (1999-11), pages 755-760, XP002350372 abstract page 756, right-hand column, paragraph 2 - page 757, left-hand column, paragraph 1; figure 1</td>
<td>1,18-21, 24-37</td>
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<td>A</td>
<td>WO 01/32927 A (INCYTE GENOMICS, INC; SORNASSE, THIERRY; SEILHAMER, JEFFREY, J; WATSON) 10 May 2001 (2001-05-10) Seq Id No 281. Table 1, page 23. abstract</td>
<td>1,18-21, 24-37</td>
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<td>A</td>
<td>DE 42 43 648 A1 (BOEHRINGER MANNHEIM GMBH, 68305 MANNHEIM) 7 July 1994 (1994-07-07) example 4</td>
<td>1,18-21, 24-37</td>
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<td>A</td>
<td>DATABASE EMBL 4 May 2002 (2002-05-04), XP002366938 Database accession no. BQ230791 SEQ ID No: 25 has 99.85 % identity (100.00 % ungapped) over 669 (q:s=584-1252:1-669) with subject EM_EST:BQ230791 abstract</td>
<td>1,18-21, 24-37</td>
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</table>
INTERNATIONAL SEARCH REPORT

Box 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 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 fee, this Authority did not invite payment of any additional fee.

3. X 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.:

   1, 18-21, 24-37 all partially, concerning inventions 1 and 4.

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.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 22, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 2: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 23, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 3: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 24, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 4: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 25, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 5: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 353, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 6: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 386, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Inventions 7 to 26: Claims 2 (partially), 18-21 (partially), 24-37 (partially)
Polynucleotides comprising Seq Id Nr n, with n from 130 to 149, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides.

Invention 27: Claims 3 (partially), 4, 5, 15-37 (partially)

Polypeptides comprising Seq Id Nr 301, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 28: Claims 3 (partially), 6, 7, 15-37 (partially)

Polypeptides comprising Seq Id Nr 302, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 29: Claims 3 (partially), 8, 9, 15-37 (partially)

Polypeptides comprising Seq Id Nr 303, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 30: Claims 3 (partially), 10, 11, 15-37 (partially)

Polypeptides comprising Seq Id Nr 304, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 31: Claims 3 (partially), 15-37 (partially)

Polypeptides comprising Seq Id Nr 325, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 32: Claims 3 (partially), 15-37 (partially)

Polypeptides comprising Seq Id Nr 354, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 33: Claims 3 (partially), 15-37 (partially)
Polypeptides comprising Seq Id Nr 355, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 34: Claims 3 (partially), 15-37 (partially)

Polypeptides comprising Seq Id Nr 356, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 35: Claims 3 (partially), 15-37 (partially)

Polypeptides comprising Seq Id Nr 387, antibodies thereto, kits comprising said polynucleotides or antibodies and diagnostic and therapeutical applications of said polypeptides.

Invention 36: Claims 12 (partially), 28-37 (partially)

Oligonucleotides comprising Seq Id Nr 379 and diagnostic and therapeutical applications of said oligonucleotides.

Invention 37: Claims 12 (partially), 28-37 (partially)

Oligonucleotides comprising Seq Id Nr 382 and diagnostic and therapeutical applications of said oligonucleotides.

Invention 38: Claims 12 (partially), 28-37 (partially)

Oligonucleotides comprising Seq Id Nr 385 and diagnostic and therapeutical applications of said oligonucleotides.

Invention 39: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 377.

Invention 40: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 378.

Invention 41: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 380.
Invention 42: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 381.

Invention 43: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 383.

Invention 44: Claims 13 and 14 (both partially)

Oligonucleotide having Seq Id Nr 384.
<table>
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<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
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<tr>
<td></td>
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<td>CA 2388511 A1</td>
<td>10-05-2001</td>
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<td>EP 1255859 A2</td>
<td>13-11-2002</td>
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<td>JP 2004507206 T</td>
<td>11-03-2004</td>
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