Title: DIGITAL PROFILING OF POLYNUCLEOTIDE POPULATIONS

Abstract: The invention provides methods and compositions for hybridization-based assays that employ oligonucleotide tags, wherein probes specific for the same target polynucleotide are labeled with a plurality of different oligonucleotide tags. When probes are used in conjunction with a microarray, or like, readout platform, containing hybridization sites of tag complements, assay of a target polynucleotide results in a signal being generated from any of a plurality hybridization sites with predetermined addresses and the number of such sites generating a signal is proportional to the relative amount of the target polynucleotide in a population, test sample, or reaction volume, as the case may be. The invention provides methods and compositions for measuring amounts of selected target polynucleotides in a sample and for providing a digital readout of such amounts. Statistical confidence in measurements made by the present invention may be increased as much as desired by increasing the size of the sample of successfully hybridized and selected probes from which signals are generated.
before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

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.

(88) Date of publication of the international search report: 26 January 2006
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/04
US Cl. : 435/6, 91.1, 91.2; 536/23.1, 24.3, 24.33

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. : 435/6, 91.1, 91.2; 536/23.1, 24.3, 24.33

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

<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>WO 97/0365 A1 (AFFYMAX) 20 March 1997 (20.03.1997), page 5, lines 15-17; page 4, lines 12-13.</td>
<td>8-10</td>
</tr>
<tr>
<td>X</td>
<td>BRENNER et al. Gene expression analysis by massively parallel signature sequencing (MPSS) on micro bead arrays. Nature Biotechnology. 18 June 2000, Vol. 18, pages 630-634, especially page 630, 2nd column, bottom paragraph, page 631, 1st column, 1st paragraph; Figure 1; page 631, 2nd column, 1st paragraph; page 634, 1st column, 1st paragraph; and Abstract.</td>
<td>1-5, 8-10, and 12-17</td>
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<td>Y</td>
<td>US 2003/0104436 A1 (MORRIS et al.) 5 June 2003, sections [0065], [0056], [0091], [0110], and [0121].</td>
<td>1-17</td>
</tr>
<tr>
<td>Y</td>
<td>US 5,854,033 (LIARDI, P.M.) 29 December 1998, column 2, lines 60-66; column 3, line 9; column 5, lines 17-19; Figure 1, column 2, lines 56-57; column 7, lines 8-9; and Figure 10.</td>
<td>1-17</td>
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Additional information:

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

Special categories of cited documents:

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- "Z" document member of the same patent family

Date of the actual completion of the international search
07 September 2005 (07.09.2005)

Date of mailing of the international search report
18 November 2005 (18.11.2005)

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Continuation of B. FIELDS SEARCHED Item 3:
Patent Databases (USPT, USPGP, EPO, IPO, DERWENT)
NPL (PubMed)
search terms: digital profiling, oligonucleotide tag, RCA, rolling circle amplification, microarray, hybridization.