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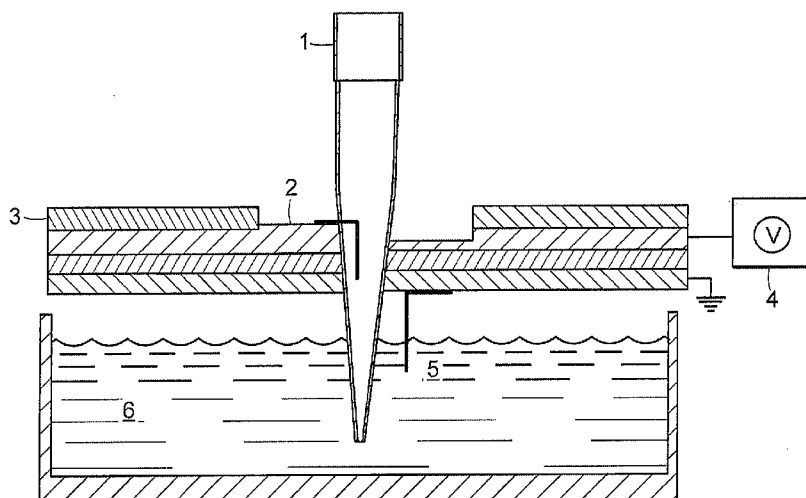
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[Continued on next page]

(54) Title: A METHOD AND APPARATUS FOR SPATIALLY CONFINED ELECTROPORATION



(57) Abstract: The invention provides hollow-tip-electrodes for spatially localized delivery of substances to one or more biological targets present in a population comprising target and non-target molecules, macromolecules, and/or cells. The invention also provides electrode plates for receiving one or more of such tips, tip-electrode plates comprising electrode plates comprising one or more electrode tips, and systems comprising tip-electrodes and containers for containing one or more biological targets, e.g., such as molecules, macromolecules, and/or cells. The invention further provides methods for using such systems and components thereof. In one preferred aspect, the systems are used for spatially confined electroporation of cells and cells structures. The invention facilitates high throughput screening of agents (e.g., such as drugs) that act on intracellular targets.

WO 2007/039783 A3



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.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61N1/30 A61B5/04 A61N1/32

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)

A61N A61B

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

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 6 208 893 B1 (HOFMANN G&Uuml ET AL) 27 March 2001 (2001-03-27)</p> <p>column 9, line 7 - column 10, line 14; claims 1,5,19,25; figures 1,10-12</p> <p>----- -/--</p>	<p>1,2,4,7, 8,10,12, 15,29, 31-33, 35,43, 44,47, 55-57, 70, 136-139, 141</p>

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in 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 document but published on or after the international filing date

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"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.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	WO 01/43817 A1 (UNIVERSITY OF SOUTH FLORIDA) 21 June 2001 (2001-06-21) page 6, line 10 - page 7, line 29; claim 1; figure 4 -----	1,2,4,7, 8,10,12, 15,29, 31-33, 35,38, 39,43, 44,47, 55-57, 70, 136-139
X	WO 95/23211 A1 (RAMOT-UNIV. AUTHORITY FOR APPLIED RESEARCH AND IND; SHOSHAN, HERBERT,) 31 August 1995 (1995-08-31) page 4, line 16 - page 5, line 15; claim 1; figure 1 -----	29, 31-33, 35,136, 137,139, 141,199, 200,204, 205,207
X	US 6 241 666 B1 (POMERANZ MARK L ET AL) 5 June 2001 (2001-06-05) column 2, line 31 - column 3, line 34; claim 1 -----	1-3,10, 14
X	US 2003/014081 A1 (BERNABEI GIAN FRANCO) 16 January 2003 (2003-01-16) abstract; claim 1; figure 2b -----	29, 31-33,35
X A	US 6 278 895 B1 (BERNARD ROBERT M) 21 August 2001 (2001-08-21) the whole document -----	29, 31-33,35 1-28,30, 34, 36-198
X	WO 03/013647 A (CYTO PULSE SCIENCES, INC) 20 February 2003 (2003-02-20) page 29, lines 19-22 -----	213
Y A	US 6 326 177 B1 (SCHOENBACH KARL H ET AL) 4 December 2001 (2001-12-04) abstract -----	213 214-221
Y,P	WO 2004/039489 A (CELLECTRICON AB; WIGSTROM, JOAKIM; SINCLAIR, JON) 13 May 2004 (2004-05-13) the whole document -----	213
A	US 2002/076689 A1 (FARB DAVID H ET AL) 20 June 2002 (2002-06-20) the whole document -----	199-212

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/004477

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. ☐ 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.
- ☐ 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: 1-198

Device/Method comprising an electrode plate having opening for electrodes. These electrodes having a lumen for receiving an electrically conductive medium and an electrically conductive surface for coupling to a voltage or current generator.

2. claims: 199-212

Method of screening for an agent which alters an interaction between a first intracellular component and a second intracellular component, comprising :
contacting a cell comprising the first intracellular component and the second intracellular component with the agent;
exposing the cell to a focused electric field using a tip electrode of claim 1 under conditions for generating pores in the cell, and
detecting a change in the interaction.

3. claims: 213-221

A method for screening for an agent comprising the intracellular component with a candidate binding agent;
exposing the cell to a focused electric field using a tip electrode of claim 1 under conditions for generating pores in the cell, and
detecting binding of the agent to the component.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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