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(54) Development and use of fluorescent probes of unbound analytes

(57) A method for high throughput screening of probes is described. These probes are useful for characterization and measurement of unbound metabolites in a fluid sample, particularly characterization and measurement of levels of unbound free fatty acids. By practice of the disclosed invention, a profile of unbound metabolites can be determined for an individual which can be used to determine the individual's relative risk for disease such as stroke, cardiac disease and cancer.

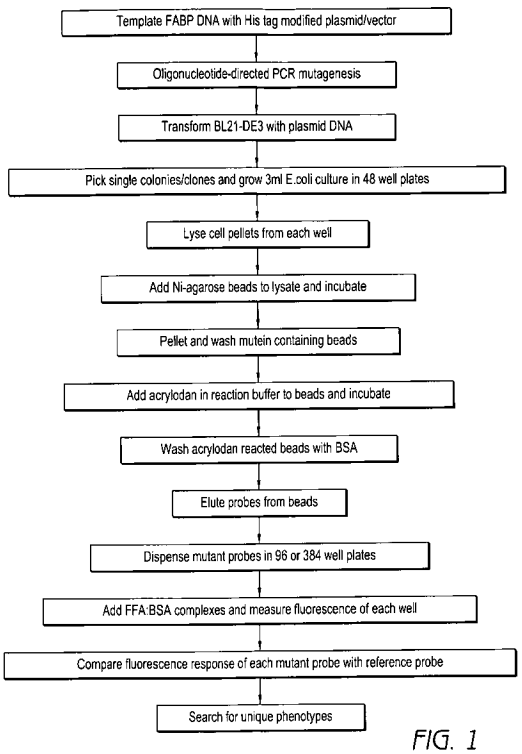

FIG. 1

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EUROPEAN SEARCH REPORT

Application Number
EP 10 17 7671

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 98/57171 A (MEDICAL BIOLOGY INSTITUTE; KLEINFELD, ALAN, M) 17 December 1998 (1998-12-17) * page 4, last paragraph - page 5, paragraph 1 *	1-7, 9-12,15	INV. G01N33/92 G01N33/58 G01N33/533 G01N33/72
X	RICHIERI GARY V ET AL: "Kinetics of fatty acid interactions with fatty acid binding proteins from adipocyte, heart, and intestine", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 19, 1996, pages 11291-11300, XP002347631, ISSN: 0021-9258 * figure 5a *	1-7, 9-12,15	
A	OKAMURA Y ET AL: "Anti-bilirubin monoclonal antibody III. Preparation and properties of monoclonal antibodies to unconjugated bilirubin-IXalpha", BIOCHIMICA ET BIOPHYSICA ACTA - GENERAL SUBJECTS, ELSEVIER SCIENCE PUBLISHERS, NL, vol. 1073, no. 3, 9 April 1991 (1991-04-09), pages 538-542, XP023577392, ISSN: 0304-4165, DOI: 10.1016/0304-4165(91)90227-8 [retrieved on 1991-04-09] * page 541, right-hand column, last paragraph - page 541, left-hand column, paragraph 1; figure 5 *	1-12,15	

TECHNICAL FIELDS SEARCHED (IPC)
G01N

~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
Munich	12 January 2012	Lanzrein, Markus

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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EPO FORM 1503 03.82 (P04C01)

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Application Number
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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☒ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

1-12, 15(all partially)

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

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LACK OF UNITY OF INVENTION
SHEET B

Application Number
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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-7, 9-12, 15(all partially)

The FABP probe comprising mutations at positions 102 and 72 (first mutant shown in Table 3; method for determining free fatty acid with the said probe

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2-836. claims: 1-12, 15(all partially)

The FABP probe derived from clones listed in Tables 3-7, beginning with the second mutant; method for determining free fatty acid with the said probe

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837. claims: 13, 14

Method for determining a profile of unbound metabolites in body fluids with a combination of probes producde by a high throughput method comprising the steps of generating a library of FABP mutants, purifying the proteins and binding them to a solid matrix, associating the proteins with fluorophores to produce probes and retrieving the probes from the solid matrix.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 10 17 7671

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

12-01-2012

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9857171 A	17-12-1998	AU 3395697 A	30-12-1998
		WO 9857171 A1	17-12-1998

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

专利名称(译)	开发和使用未结合分析物的荧光探针		
公开(公告)号	EP2385375A3	公开(公告)日	2012-02-22
申请号	EP2010177671	申请日	2005-03-21
申请(专利权)人(译)	FFA科学，律师事务所		
当前申请(专利权)人(译)	FFA科学，律师事务所		
[标]发明人	KLEINFELD ALAN MARC HUBER ANDREW HENRY KAMPF JAMES PATRICK ZHU BAOLONG KWAN THOMAS		
发明人	KLEINFELD, ALAN, MARC HUBER, ANDREW, HENRY KAMPF, JAMES, PATRICK ZHU, BAOLONG KWAN, THOMAS		
IPC分类号	G01N33/92 G01N33/58 G01N33/533 G01N33/72 C12P19/34 C12P21/02 C12Q1/68		
CPC分类号	C12P21/02 G01N33/533 G01N33/582 G01N33/728		
优先权	60/555224 2004-03-22 US		
其他公开文献	EP2385375A2		
外部链接	Espacenet		

摘要(译)

描述了用于探针的高通量筛选的方法。这些探针可用于表征和测量流体样品中未结合的代谢物，特别是表征和测量未结合的游离脂肪酸的水平。通过实施所公开的发明，可以确定个体的未结合代谢物的概况，其可以用于确定个体的疾病相对风险，例如中风，心脏病和癌症。

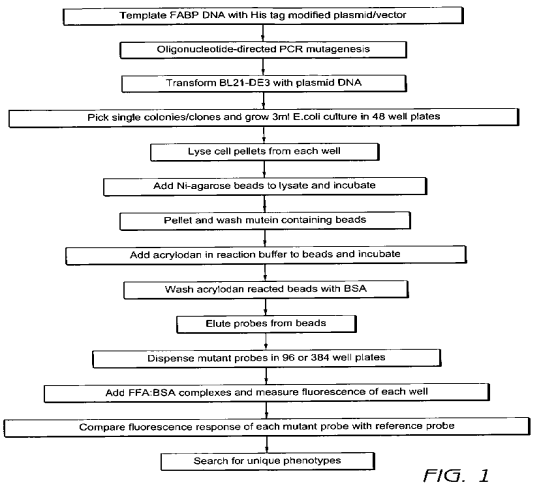

FIG. 1