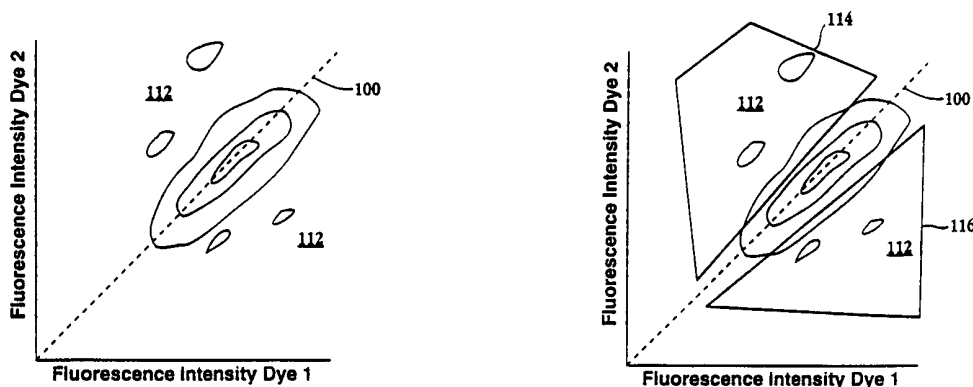




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/US99/00666</p> <p>(22) International Filing Date: 8 January 1999 (08.01.99)</p> <p>(30) Priority Data: 09/005,222 9 January 1998 (09.01.98) US 09/130,446 6 August 1998 (06.08.98) US</p> <p>(71) Applicant (for all designated States except US): LYNX THERAPEUTICS, INC. [US/US]; 3832 Bay Center Place, Hayward, CA 94545 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): ALBRECHT, Glen [US/US]; 1113 Oliver Street, Redwood City, CA 94061 (US). BRENNER, Sydney [GB/GB]; 17 B St. Edwards Passage, Cambridge CB2 3PJ (GB). DUBRIDGE, Robert [US/US]; 825 Holly Road, Belmont, CA 94002 (US).</p> <p>(74) Agents: ASHTON, Nina, M.; Cooley Godward LLP, Five Palo Alto Square, 3000 El Camino Real, Palo Alto, CA 94306-2155 (US) et al.</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 30 September 1999 (30.09.99)</p>

(54) Title: SOLID PHASE SELECTION OF DIFFERENTIALLY EXPRESSED GENES



(57) Abstract

The invention provides a method and materials for monitoring and isolating differentially expressed genes. In accordance with the method of the invention, differently labeled populations of DNAs from sources to be compared are competitively hybridized with reference DNA cloned on solid phase supports, e.g. microparticles, to provide a differential expression library which, in the preferred embodiment, may be manipulated by fluorescence-activated cell sorting (FACS). Monitoring the relative signal intensity of the different fluorescent labels on the microparticles permits quantitative analysis of expression levels relative to the reference DNA. The invention also provides a method for identifying and isolating rare genes. Populations of microparticles having relative signal intensities of interest can be isolated by FACS and the attached DNAs identified by sequencing, such as with massively parallel signature sequencing (MPSS), or with conventional DNA sequencing protocols.

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INTERNATIONAL SEARCH REPORT

Inter. Appl. No.

PCT/US 99/00666

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68

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)

IPC 6 C12Q

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>SCHENA M ET AL: "QUANTITATIVE MONITORING OF GENE EXPRESSION PATTERNS WITH A COMPLEMENTARY DNA MICROARRAY" SCIENCE, vol. 270, no. 5235, 20 October 1995 (1995-10-20), pages 467-470, XP000644675 ISSN: 0036-8075 cited in the application</p>	27-29
Y	<p>see whole doc, esp. p.468, col.3</p>	1-26, 30-60
Y	<p>WO 96 12039 A (LYNX THERAPEUTICS INC) 25 April 1996 (1996-04-25) cited in the application see whole doc., esp. claims 43ff</p>	1-26, 30-60

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/00666

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DERISI J.L. ET AL.,: "Exploring the metabolic and genetic control of gene expression on a genomic scale" SCIENCE, vol. 278, - 24 October 1997 (1997-10-24) pages 680-686, XP002110854 the whole document</p>	27-29
A	<p>VAN NESS J ET AL: "A VERSATILE SOLID SUPPORT SYSTEM FOR OLIGODEOXYNUCLEOTIDE PROBE -BASED HYBRIDIZATION ASSAYS" NUCLEIC ACIDS RESEARCH, vol. 19, no. 12, 25 June 1991 (1991-06-25), pages 3345-3350, XP000208399 ISSN: 0305-1048 the whole document</p>	-

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Information on patent family members

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