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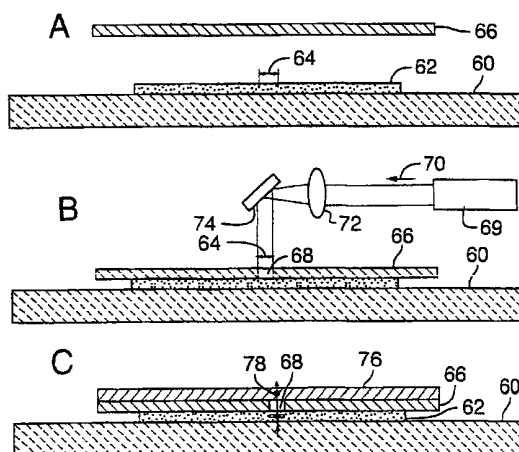
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(54) Title: TRANSFER MICRODISSECTION



(57) Abstract: The present disclosure concerns methods, systems, and devices for analyzing a biological material, such as a cellular or other specimen. In one disclosed example, the method selectively transfers biomolecules from a target region of interest in a biological sample (such as a tissue section). The transfer may occur, for example, by selectively focally altering a characteristic of a transfer layer adjacent the target region, such that the biomolecules can move through the altered area of the transfer layer. In particular examples, the transfer layer is altered by focally increasing a permeability of the transfer layer, for example by removing a focal portion of the transfer layer, and transporting the biomolecules through the altered region of the transfer layer, to microdissect the biomolecules of interest from the biological sample. In yet other embodiments, the microdissected biomolecules can be applied to an analysis substrate containing an identification molecule, such as a nucleic acid array, layered expression scan, or wells containing antibodies. Transfer microdissection allows biomolecules from regions of interest in the biological specimen to be selectively analyzed. For example, nests of highly atypical or metastatic cells in a tumor section can be analyzed for differential expression of certain proteins.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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Minimum documentation searched (classification system followed by classification symbols)

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMMERT-BUCK M R ET AL: "LASER CAPTURE MICRODISSECTION" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE., US, vol. 274, no. 5289, 8 November 1996 (1996-11-08), pages 998-1001, XP000644727 ISSN: 0036-8075 cited in the application the whole document ---	1-77
X	WO 97 13838 A (EMMERT BUCK MICHAEL ;LINEHAN W MARSTON (US); US HEALTH (US); BONNE) 17 April 1997 (1997-04-17) cited in the application the whole document --- -/--	1-77



Further documents are listed in the continuation of box C



Patent family members are listed in annex.

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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	ENGLERT CHAD R ET AL: "Layered expression scanning: Rapid molecular profiling of tumor samples" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 60, no. 6, 15 March 2000 (2000-03-15), pages 1526-1530, XP002156603 ISSN: 0008-5472 cited in the application the whole document ---	1-77
X	BANKS R E ET AL: "THE POTENTIAL USE OF LASER CAPTURE MICRODISSECTION TO SELECTIVELY OBTAIN DISTINCT POPULATIONS OF CELLS FOR PROTEOMIC ANALYSIS - PRELIMINARY FINDINGS" ELECTROPHORESIS, WEINHEIM, DE, vol. 20, no. 4/5, April 1999 (1999-04), pages 689-700, XP000925546 ISSN: 0173-0835 the whole document ---	1-77
P,X	WO 01 07915 A (EMMERT BUCK MICHAEL R ;US HEALTH (US)) 1 February 2001 (2001-02-01) cited in the application the whole document -----	1-77

INTERNATIONAL SEARCH REPORT

Information on patent family members

In. ational Application No

PCT/US 01/08095

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9713838	A	17-04-1997	US 5843657 A	01-12-1998
			AU 716979 B2	16-03-2000
			AU 7663396 A	30-04-1997
			CA 2233614 A1	17-04-1997
			EP 0862612 A1	09-09-1998
			JP 2000500325 T	18-01-2000
			US 6251516 B1	26-06-2001
			WO 9713838 A1	17-04-1997
			US 6251467 B1	26-06-2001
			US 6204030 B1	20-03-2001
			US 2001031481 A1	18-10-2001
			US 6010888 A	04-01-2000
WO 0107915	A	01-02-2001	AU 6609100 A	13-02-2001
			WO 0107915 A2	01-02-2001