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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: SYSTEMS AND METHODS FOR SCREENING PHARMACEUTICAL CHEMICALS

(57) Abstract: A method for obtaining a response of a tissue model system to an activator includes contacting a bio-artificial tissue model system with an activator and measuring cellular mechanical response thereto of at least one of contractile force and tissue stiffness. A method for obtaining a response of a tissue model system to an activator includes contacting a bio-artificial tissue model system with an activator and measuring cellular mechanical response thereto of at least one of contractile force and hysteresis.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/25761

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 5/00, 5/02, 5/06; A61M 1/10

US CL : 435/325, 347; 623/3.1

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. : 435/325, 347; 623/3.1

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)
STN - CAPLUS, Medline, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,326,357 A (KANDEL) 05 July 1994 (05.07.1994), see entire document.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91
Y	US 4,593,042 A (LIANG) 03 June 1986 (03.06.1986), columns 9-13.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91
Y	US 5,038,795 A (ROUSH et al) 13 August 1991 (13.08.1991) see entire document.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91
Y	US 4,705,785 A (SCHWEDNER et al) 10 November 1987 (10.11.1987), column 13.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91

☒ Further documents are listed in the continuation of Box C.

☐ See patent family 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 application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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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INTERNATIONAL SEARCH REPORT

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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.
Y	US 5,665,391 A (LEA) 09 September 1997 (09.09.1997), see entire document.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91
Y	US 5,706,815 A (SARVAZYAN et al.) 13 January 1998 (13.01.1998), see entire document.	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91
Y	US 5,464,853 A (CHAN et al) 07 November 1995 (07.11.1995), columns 16 and 17	1-11, 14, 16-21, 31-34, 50, 53-56, 60-62, 66, 71-73, 87-89, 91

INTERNATIONAL SEARCH REPORT

International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 12,13,15,22-30,35-49,51,52,57-59,63-65,67-70,74-86,90 and 92-105
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:
Please See Continuation Sheet
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

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.

INTERNATIONAL SEARCH REPORT

PCT/US02/25761

Continuation of Box I Reason 2:

Claims 12, 15, 51, 52, 57, 58, 65, 75, 92-95, and 100-104 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): each of the claims, or claims from which they depend, recites one or more terms that lack antecedent basis. Consequently, the claims cannot be interpreted in a meaningful way for search purposes.

Claims 13, 59, 74, 90, and 105 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): the phrase "*comprises cells of extracellular matrix*" in claim 13 does not make sense because cells cannot be extracellular matrix; claim 59 recites making a comparison of the profile of a pharmaceutical known to be effective against cells but does not recite what the profile is compared to; claims 74 and 90 recite "*the tissue is muscle cells*" but a tissue is comprised of more than one type of cell; claim 105 recites a method of optimizing tissue culture conditions for constructing implantable artificial cardiac tissue but provides no method steps and the claim is not a grammatically complete sentence.

Claims 22-30 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): the language recited in claim 22 is confusing because the meaning of the phrase "*based on reconstituted model muscle and non-muscle tissue mechanical measurements of the response of a tissue model*" is unclear and "*said reconstituted cell matrix*" lacks antecedent basis in the claim.

Claims 35, 36, and 83-86 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): it is not clear an "*activator*" or "*cell activator*" is or in what way it activates a cell.

Claims 37-49 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): the preamble of claim 37 recites a method of managing a library of pharmaceuticals but the method steps recited does not result in the management of a library of pharmaceuticals.

Claims 63 and 64 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): it is not clear which of the forces in claim 60 they are limiting.

Claims 67-70 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): in claim 67, the meaning of "*provided with a support*" is not searchable because it is not clear what type of support is provided (e.g. structural or nutritional).

Claims 76-86 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): claim 76 recites "*comprising cells and ECM arranged in a membrane*" but it is not clear if this means that the two recited components form a membrane or if they are arranged in a membrane made of other materials such as thin plastic or other sheet material.

Claims 96-99 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): claim 96 recites a method of culturing a cardiac tissue model but provides no method steps for culturing the cardiac tissue model and it is not clear what a cardiac tissue model comprises. Consequently, claims 96-99 cannot be searched.