

(19) World Intellectual Property  
Organization  
International Bureau

(43) International Publication Date  
12 December 2024 (12.12.2024)



(10) International Publication Number  
**WO 2024/254436 A3**

(51) International Patent Classification:  
C12M 3/06 (2006.01)

(21) International Application Number:  
PCT/US2024/032983

(22) International Filing Date:  
07 June 2024 (07.06.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
63/506,691 07 June 2023 (07.06.2023) US

RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**  
— with international search report (Art. 21(3))

**(88) Date of publication of the international search report:**  
08 May 2025 (08.05.2025)

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ,

(54) Title: BIO-ENGINEERED HUMAN PROSTATE GLAND AND DISEASE MODEL

(57) Abstract: Microfluidic devices, organ-on-a-chip platforms (e.g. mimicking the human prostate gland), and uses thereof are described herein. The microfluidic device includes at least two layers and a porous membrane therebetween. Each layer includes a channel, and the first channel and the second channel are aligned such that a first region of a first channel overlaps with a region of the second channel, and a second region of the first channel does not overlap a second region of the second channel. A disease model using the microfluidic devices includes (i) placing a first type of cells in the first channel and (ii) flowing a first cell culture medium through the first channel. Optionally, in step (i) a second type of cells in the second channel and in step (ii) a second cell culture medium flows through the second channel. The microfluidic devices can be used in drug screening and testing.



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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/32983

## A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C12M 3/06 (2024.01)

ADD. C12M 1/12, C12N 5/071, B01L 3/00 (2024.01)

CPC - INV. C12M 23/16

ADD. C12M 25/02, C12N 5/0697, B01L 3/502715

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

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

See Search History document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                         | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | US 2018/0119081 A1 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 03 May 2018 (03.05.2018) para [0012]; [0016]; [0024]; [0025]; [0026]; [0028]; [0029]; [0030]; [0031]; [0032]; [0037]; [0042]; [0045]; [0051] | 1-19, 39-42           |
| A         | US 2011/0250585 A1 (INGBER et al.) 13 October 2011 (13.10.2011) Entire document                                                                                                                            | 1-19, 39-42           |

☐ 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

"D" document cited by the applicant in the international application

"E" earlier application or patent but 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

20 August 2024 (20.08.2024)

Date of mailing of the international search report

NOV 01 2024

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/32983

## Box No. 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 No. 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:  
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-19, 39-42, directed to a microfluidic device and organ-on-a-chip platform.

Group II, claims 20-38, directed to a method for constructing a disease model and drug screening using a microfluidic device.

The inventions listed as Groups I-II do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

----- See Extra Pages -----

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 additional fees, this Authority did not invite payment of additional fees.
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.:  
1-19, 39-42

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Box No. III Observations where unity of invention is lacking:

Special technical features:

Group I has the special technical feature of a microfluidic device and organ-on-a-chip platform, that is not required by Group II.

Group II has the special technical feature of a method for constructing a disease model and drug screening using a microfluidic device, that is not required by Group I.

Common technical features:

Groups I-II share the common technical feature of:

a microfluidic device comprising:

at least two layers, each layer comprising one, two or more channels; and

a first porous membrane,

wherein the first layer is in parallel with the second layer,

wherein the first porous membrane is adjacent to each of and between the first and second layers,

wherein the microfluidic device comprises a material exchange area,

wherein within the material exchange area, a first region of a first channel overlaps with a second region of a second channel, and

wherein a third region of the first channel does not overlap with any region of the second channel in the material exchange area

However, this shared technical feature does not represent a contribution over prior art, because this shared technical feature is obvious over US 2011/0250585 A1 to Ingber et al. (hereinafter 'Ingber').

Ingber teaches a microfluidic device comprising:

at least two layers, each layer comprising a channel (para [0066] - "the present disclosure is directed to device and method of use in which the device includes a body having a central microchannel separated by one or more porous membranes. The membrane(s) are configured to divide the central microchannel into two or more closely apposed parallel central microchannels"); and

a first porous membrane (para [0066] - "the present disclosure is directed to device and method of use in which the device includes a body having a central microchannel separated by one or more porous membranes. The membrane(s) are configured to divide the central microchannel into two or more closely apposed parallel central microchannels"),

wherein the first layer is in parallel with the second layer (para [0066]),

wherein the first porous membrane is adjacent to each of and between the first and second layers (para [0066]),

wherein the microfluidic device comprises a material exchange area,

wherein within the material exchange area, a first region of a first channel overlaps with a second region of a second channel (para

[0120] - "In another example, the device 200 utilizes the porous membrane 208, whereby lung cells are grown on one side of the

membrane 208 and endothelial cells are maintained on the other side of the membrane 208. During the operation of the device 200,

these two cells layers communicate with each other through passage of chemical and molecular cues through the pores on the

membrane 208"), but does not expressly teach wherein a third region of the first channel does not overlap with any region of the second

channel in the material exchange area. It would have been obvious to one of ordinary skill in the art, during the course of ordinary

experimentation, to apply a region of the first channel that does not overlap with the second channel in order to compare the effects of

the tissue interface taught by Ingber to a control population of cells within the channel that do not interface with tissue in the second

channel.

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I-II inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.