

**PATENT COOPERATION TREATY**

**TRANSLATION**

From the  
INTERNATIONAL SEARCHING AUTHORITY

**PCT**

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing (day/month/year)	<b>17.07.2018</b>
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Applicant's or agent's file reference <b>PC-25345</b>	<b>FOR FURTHER ACTION</b> See paragraph 2 below
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International application No. <b>PCT/JP2018/016126</b>	International filing date (day/month/year) <b>19.04.2018</b>	Priority date (day/month/year) <b>20.04.2017</b>
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International Patent Classification (IPC) or both national classification and IPC  
**C12N15/12 (2006.01) i, A61K35/42 (2015.01) i, A61L27/38 (2006.01) i, A61P11/00 (2006.01) i, A61P43/00 (2006.01) i, C12N5/071 (2010.01) i, C12N5/16 (2006.01) i, C12N15/63 (2006.01) i**

Applicant  
**KEIO UNIVERSITY**

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
  - the international application in the language in which it was filed
  - a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2.  This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
  - a.  forming part of the international application as filed:
    - in the form of an Annex C/ST.25 text file.
    - on paper or in the form of an image file.
  - b.  furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
  - c.  furnished subsequent to the international filing date for the purposes of international search only:
    - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
    - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4.  In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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<b>Box No. V</b>	<b>Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</b>
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1. Statement									
Novelty (N)		<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 10%; padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;">1-9</td> <td style="width: 10%; text-align: right; padding: 2px;">YES</td> </tr> <tr> <td style="padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;">10, 11</td> <td style="text-align: right; padding: 2px;">NO</td> </tr> </table>	Claims	1-9	YES	Claims	10, 11	NO	
Claims	1-9	YES							
Claims	10, 11	NO							
Inventive step (IS)		<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 10%; padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;">1-9</td> <td style="width: 10%; text-align: right; padding: 2px;">YES</td> </tr> <tr> <td style="padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;">10, 11</td> <td style="text-align: right; padding: 2px;">NO</td> </tr> </table>	Claims	1-9	YES	Claims	10, 11	NO	
Claims	1-9	YES							
Claims	10, 11	NO							
Industrial applicability (IA)		<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 10%; padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;">1-11</td> <td style="width: 10%; text-align: right; padding: 2px;">YES</td> </tr> <tr> <td style="padding: 2px;">Claims</td> <td style="border-bottom: 1px solid black; padding: 2px;"></td> <td style="text-align: right; padding: 2px;">NO</td> </tr> </table>	Claims	1-11	YES	Claims		NO	
Claims	1-11	YES							
Claims		NO							

2. Citations and explanations:	
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Document 1: WO 2016/143803 A1 (KYOTO UNIVERSITY) 15 September 2016, page 34, lines 1-8 & US 2018/0051256 A1, paragraphs [0164], [0165] & EP 3266864 A1

Document 2: WO 2015/178496 A1 (NATIONAL INSTITUTE OF ADVANCED INDUSTRIAL SCIENCE AND TECHNOLOGY) 26 November 2015, page 1, lines 9-16, page 21, lines 25-29 (Family: none)

A. The invention as in claims 10 and 11 lacks novelty and does not involve an inventive step in the light of document 1 cited in the ISR.

Document 1 (page 34, lines 1-8, etc.) indicates that type II alveolar epithelial cells is administered as a formulation to patients with broken alveoli.

The type II alveolar epithelial cells disclosed in document 1 is not produced in the production method set forth in any one of claims 6-9 of the present application, but even after taking into account the disclosures of the description of the present application and common technical knowledge, it is not considered that

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

the alveolar epithelial cells obtained in the production method set forth in any one of claims 6-9 of the present application has a difference that can distinguish themselves from the alveolar epithelial cells disclosed in document 1.

B. The invention as in claims 10 and 11 lacks novelty and does not involve an inventive step in the light of document 2 cited in the ISR.

Document 2 (page 21, lines 25-29, etc.) discloses alveolar epithelial type I cells and alveolar epithelial type II cells, and for the same reason discussed in section A, the alveolar epithelial cells according to claim 10 cannot be distinguished from the alveolar epithelial type I cells or alveolar epithelial type II cells disclosed in document 2, as a product.

Furthermore, although document 2 does not explicitly indicate that the alveolar epithelial cells are used as cell pharmaceuticals, as disclosed in document 2 (page 1, lines 9-16), it is common technical knowledge that tissue cells are used as cell pharmaceuticals. Accordingly, document 2 essentially indicates that alveolar epithelial cells are used as cell pharmaceuticals, and even if this were not the case, using alveolar epithelial cells as cell pharmaceuticals would be easy for a person skilled in the art.

C. The invention as in claims 1-9 is novel and involves an inventive step in relation to documents 1 and 2 cited in the ISR.

Documents 1 and 2 do not indicate or suggest that alveolar epithelial cells are obtained from somatic

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citations and explanations supporting such statement

cells, by introducing NK2 homeobox family gene and Fox family gene for forced expression. Moreover, even a person skilled in the art could not easily conceive of the feature, on the basis of documents 1 and 2.