

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:
RESNICK, David
Nixon Peabody LLP, 100 Summer Street
Boston, Massachusetts 02110-2131
United States of America

Date of mailing (<i>day/month/year</i>) 22 August 2013 (22.08.2013)		FOR FURTHER ACTION See paragraph 2 below	
Applicant's or agent's file reference 043214071761			
International application No. PCT/US 2013/037996	International filing date (<i>day/month/year</i>) 24 April 2013 (24.04.2013)	Priority date (<i>day/month/year</i>) 24 April 2012 (24.04.2012)	
International Patent Classification (IPC) or both national classification and IPC C12N 5/07 (2010.01) C12N 5/02 (2006.01) A61K 48/00 (2006.01)			
Applicant THE BRIGHAM AND WOMEN'S HOSPITAL, INC. et al.			

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 and 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/ FIPS Russia, 123995, Moscow, G-59, GSP-5, Berezhkovskaya nab., 30-1	Date of completion of this opinion 04 July 2013 (04.07.2013)	Authorized officer O. Kolontaevskaya
Facsimile No. +7 (499) 243-33-37		Telephone No. 8(495)531-65-15

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 2013/037996

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 43*bis*.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 filed or furnished:
 - a. (means)
 - on paper
 - in electronic form
 - b. (time)
 - in the international application as filed
 - together with the international application in electronic form
 - subsequently to this Authority for the purposes of search
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 in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US 2013/037996

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

1. Statement

Novelty (N)	Claims	<u>7, 9, 10, 11, 14-25, 27, 28, 30, 32-47, 49, 50, 52-74</u>	YES
	Claims	<u>1-6, 8, 12, 13, 26, 29, 31, 48, 51</u>	NO
Inventive step (IS)	Claims	<u>7, 11, 30, 33, 34, 46, 47, 49, 50, 52-74</u>	YES
	Claims	<u>9, 10, 14-25, 27, 28, 32, 35-45</u>	NO
Industrial applicability (IA)	Claims	<u>1-74</u>	YES
	Claims	<u></u>	NO

2. Citations and explanations:

D1: US 2011/0070647 A1, 24.03.2011

D2: US 2011/0076678 A1, 31.03.2011

D3: US 2007/0190646 A1, 16.08.2007

D1 (claims) discloses a method of obtaining a pluripotent stem cells from body tissue comprising subjecting a cell to a stress. The cell is an isolated stem cell exhibiting pluripotency and expressing a stem cell marker SSEA-3 (+). The cell is present in a homogenous population of cells. The stress comprises unphysiological stress in cell culture by chemical exposure or oxygen-deprivation or physical stress or membrane damage or mechanical stimulation or active oxygen ordeprivation of essential nutrition. The pluripotent cell is cultivated for propagation of the pluripotent cell. D1 discloses a pharmaceutical composition comprising the said pluripotent stem cell. The pluripotent stem cells can be used for regeneration medicine and treatment for dysfunctional tissue or the like and they can be further used for research into cell division or tissue regeneration.

Since, the features of claims 1-6, 8, 12, 13, 26, 29, 31, 48, and 51 are disclosed in D1, the inventions of these claims do not meet the criterion of novelty.

The invention of claims 9, 10 and 27, 28 in a part of generating the pluripotent cell by of subjecting to the stress, expressing a stem cell marker Oct4 or Nanog is disclosed in D2 (claims).

Consequently, the invention of claims 9, 10 and 27, 28 does not meet the criterion of inventive step.

As regards the features of dependent claims 14-25, 32, 35-45, so into account of notoriety of different methods of exposure of the cell it is obvious for a skilled person that these parameters can be selected experimentally.

Consequently, the inventions of claims 14-25, 32, 35-45 do not meet the criterion of inventive step.

The inventions of claims 7, 11, 30, 33, 34, 46, 47, 49-50, 52-74 are not known and are not obvious for a skilled person from prior art, therefore these inventions meet the criteria of novelty and inventive step.

The inventions are industrially applicable.