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(54) Title: MYELOID LINEAGES DERIVED FROM PLURIPOTENT CELLS

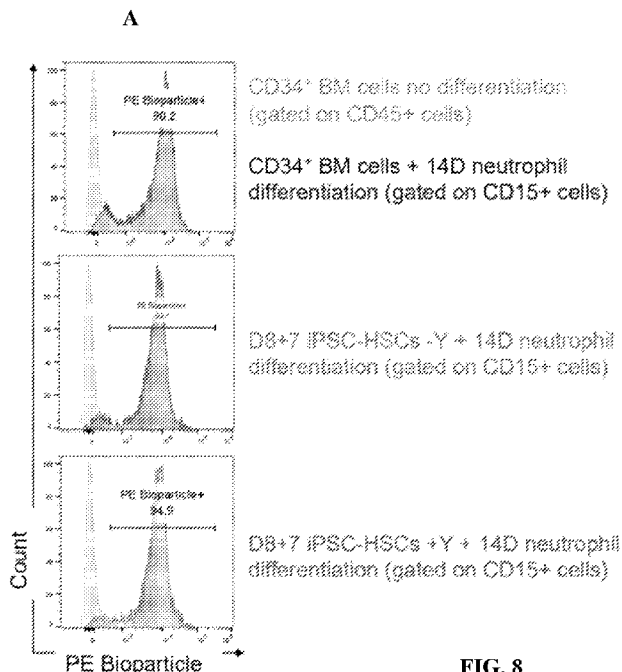


FIG. 8

(57) Abstract: The present disclosure provides for efficient ex vivo processes for generating myeloid cell lineages from human induced pluripotent stem cells (iPSCs). Cells generated according to the disclosure in various embodiments are functional and/or more closely resemble the corresponding lineage isolated from peripheral blood, bone marrow, or other tissues. The present invention in some aspects provides isolated cells and cell compositions produced by the methods disclosed herein, as well as methods for cell therapy.



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))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with sequence listing part of description (Rule 5.2(a))*

**(88) Date of publication of the international search report:**

10 May 2024 (10.05.2024)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/76109

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC - INV. C12N 5/074, C12N 5/0789 (2024.01)  
 ADD. A61P 37/04 (2024.01)

CPC - INV. C12N 5/0696, C12N 5/0647

ADD. A61P 37/04

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 --- Y	US 2020/0263139 A1 (FUJIFILM Cellular Dynamics, Inc.) 20 August 2020 (20.08.2020); entire document, especially abstract, [0002], [0005], [0006], [0008], [0021], [0036], [0069], [0168]	1-4, 6 ----- 5
Y	US 2017/0044500 A1 (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 16 February 2017 (16.02.2017); entire document, especially abstract, [0016]	5
A	US 2021/0040449 A1 (KITE PHARMA, INC.) 11 February 2021 (11.02.2021); entire document	1-6
A	US 2020/0384033 A1 (Vertex Pharmaceuticals Incorporated) 10 December 2020 (10.12.2020); entire document	1-6

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

“&” document member of the same patent family

Date of the actual completion of the international search

19 January 2024

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/76109

**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.: 7-32, 36-39  
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 1-6, directed to a method of preparing a sample.

Group II: Claims 33-35, directed to a composition comprising a myeloid lineage that is HLA-Aneg.

The inventions listed as Groups I-II do not relate to a single general inventive concept 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 Supplemental Box\*\*\*\*

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.:  
1-6

**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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 23/76109

Continuation of Box III Observations where unity of invention is lacking

Special Technical Features:

Group I requires a method for preparing an innate myeloid lineage cell population or progenitors thereof, the method comprising: enriching for CD34+ cells from a differentiated pluripotent stem cell (PSC) population to prepare a CD34+-enriched population; inducing endothelial-to-hematopoietic transition of the CD34+-enriched cell population for at least two days, but no more than 12 days, to prepare a population comprising hematopoietic stems cells (HSCs) and/or hematopoietic stem progenitor cells (HSPCs); and differentiating the population comprising hematopoietic stems cells (HSCs) and/or hematopoietic stem progenitor cells (HSPCs) to a progenitor myeloid cell population or a myeloid cell population; not required by group II.

Group II requires composition comprising a myeloid lineage that is HLA-Aneg, homozygous for both HLA-B and HLA-C, and HLA-DPB1neg and HLA-DQB1neg, and optionally further homozygous for HLA-DRB1; not required by group I.

Common Technical Features:

Groups I and II share the technical feature of a myeloid lineage. However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is being anticipated by US 2020/0263139 A1 to FUJIFILM Cellular Dynamics, Inc. (hereinafter "FUJIFILM"). FUJIFILM teaches a myeloid lineage (abstract, "Provided herein are methods for the efficient in vitro differentiation of HLA homozygous blood cell-derived pluripotent stem cells to hematopoietic precursor cells, and the further differentiation of the hematopoietic precursor cells into HLA homozygous immune cells of various myeloid or lymphoid lineages").

As the shared technical features were known in the art, they cannot be considered common technical features that would otherwise unify the groups. Therefore, Groups I-II lack unity under PCT Rule 13.

\*Item 4 (contd): Claims 7-32 and 36-39 are held unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).