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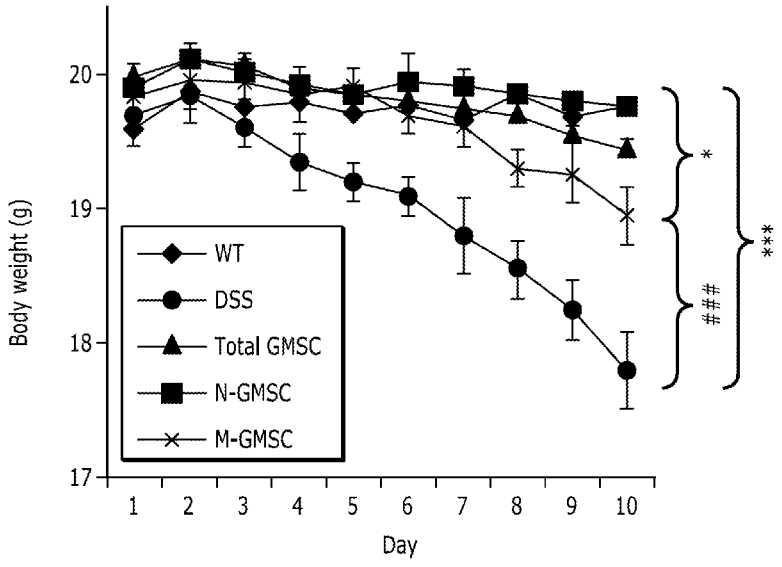
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[Continued on next page]

(54) Title: A COMPOSITION OF MESENCHYMAL STEM CELLS

FIG. 4B



(57) Abstract: This invention relates in general to a mesenchymal stem cell (MSC) therapy. This invention further relates to the isolation and applications of gingiva derived mesenchymal stem cells. More particularly, this invention relates to the isolation and applications of the neural crest derived gingiva mesenchymal stem cells and/or mesoderm derived gingiva mesenchymal stem cells. This invention also relates to a composition comprising a neural crest derived gingiva mesenchymal stem cell and/or a mesoderm derived gingiva mesenchymal stem cell. This composition may be used for wound healing and/or in the treatment of inflammatory and/or autoimmune diseases.

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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))*

(88) Date of publication of the international search report:
2 April 2015

INTERNATIONAL SEARCH REPORT

~~2014/043918 06.02.2015~~

International application No.
PCT/US 14/43918

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12N 5/077, C12N 5/0775 (2014.01)
CPC - C12N 5/0664
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)
IPC (8): C12N 5/077, C12N 5/0775 (2014.01)
CPC: C12N 5/0664

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC: C12N 5/0668

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Google patents, Google scholar, Google web, PatBase, Proquest Dialog
mesenchymal stem cell/MSC; gingiva; derived/source/origin; neural crest derived gingiva mesenchymal stem cell/NGMSC separate/disintegrate/isolate/digest; sort/flow cytometry/categorize/group; culture/grow

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	TOMAR et al. Human gingiva-derived mesenchymal stem cells are superior to bone marrow-derived mesenchymal stem cells for cell therapy in regenerative medicine. Biochem Biophys Res Commun. 12 March 2010 Vol. 393. No. 3. pp 377-383 especially, Abstract; page 377, Col. 2, para 2; page 378, Col. 2, para 4; page 378, Col. 1, para 4; page 378, Col. 1, para 9; page 381, Col. 1 para 3; page 381, Col. 2, para 1; page 381, Col. 2 para 2	1-7 --- 8-19
Y	US 2012/0128636 A1 (LE et al.) 24 May 2012 (24.05.2012) para [0013]; para [0014]; para [0040]; para [0015]; para [0041]; para [0043]; para [0067]; para [0045]	8-19

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

* 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 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	Date of mailing of the international search report
12 January 2015 (12.01.2015)	06 FEB 2015

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

~~2014/043918 06.02.2015~~

International application No.
PCT/US 14/43918

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 examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-19, drawn to a method of preparing a composition suitable for a mesenchymal stem cell (MSC) treatment of a mammal (i.e. preparing a composition comprising NGMSCs)

Group II: Claims 20-30, drawn to a method of treating a mammal using a composition comprising NGMSCs

---please see extra sheet---

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

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.

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

The inventions listed as Groups I and 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:

Special Technical Features

Group I requires preparing a composition by a. obtaining a gingival tissue, b. separating the gingival tissue into cells, c. sorting neural crest derived gingiva mesenchymal stem cells (NGMSCs), and d. preparing a composition comprising NGMSCs; not required by Group II.

Group II requires treating a mammal using a composition comprising NGMSCs, not required by Group I.

Common Technical Features

The feature shared by Groups I and II is a composition comprising neural crest derived gingiva mesenchymal stem cells (NGMSCs) that can be used to treat a mammal. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is disclosed by the article entitled "Human gingiva-derived mesenchymal stem cells are superior to bone marrow-derived mesenchymal stem cells for cell therapy in regenerative medicine" by Tomar et al. (Biochem Biophys Res Commun, 12 March 2010, Vol 393, No 3, pp 377-83) (hereinafter 'Tomar'). Tomar discloses a composition comprising gingiva mesenchymal stem cells that can be used to treat a mammal (abstract - "Gingival MSCs are easy to isolate, homogenous and proliferate faster than bone marrow MSCs without any growth factor ... we reveal that human gingiva is a better source of MSCs than bone marrow, and large number of functionally competent clinical grade MSCs can be generated in short duration for cell therapy in regenerative medicine and tissue engineering"). Although Tomar does not specifically recite a neural crest derived gingiva mesenchymal stem cell (NGMSCs), Tomar teaches that the gingiva tissues are derived from neural crest (p 381, col 1, para 3 - "Dental tissues are ecto-mesenchymal in origin and derived after epithelial-mesenchymal transition from neural crest"), thus the gingiva mesenchymal stem cells of Tomar are neural crest derived gingiva mesenchymal stem cells (NGMSCs). As the technical feature was known in the art at the time of the invention, it cannot be considered a special technical feature that would otherwise unify the groups.

Groups I and II therefore lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.