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(54) Title: AMNIOTIC FLUID-DERIVED EXTRACELLULAR VESICLES AND USES THEREOF FOR WOUND HEALING

(57) Abstract: The described invention provides compositions and methods for wound healing in a subject. The methods include administering a therapeutic amount of a pharmaceutical composition comprising extracellular vesicles from amniotic fluid and a pharmaceutically acceptable carrier.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/20229

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 35/50; A61K 45/06; C12Q 1/37 (2020.01)

CPC - A61K 35/50; A61K 45/06; C12Q 1/37

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 --- A	US 2016/0184363 A1 (University of Miami) 30 June 2016 (30.06.2016), entire document esp para [0001], [0020], [0079], [0080], [0322]	1, 3-5, 10-16 --- 2, 6 --- 7-9, 17-21
Y	WO 2007/137342 A1 (MEDVET SCIENCE PTY. LTD) 06 December 2007 (06.12.2007), entire document esp abstract, pg 5, pg 9, pg 19	2, 6
A	WO 2017/165698 A1 (MIMEDX GROUP, INC) 28 September 2017 (28.09.2017), esp para 13	17-21
A	WO 2016/197196 A1 (Prince Henry's Institute of Medical Research Trading as the Hudson Institute of Medical Research) 15 December 2016 (15.12.2016), entire document esp para [0016], [0022]	17-21

☐ 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/20229

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 1-21, directed to a method for promoting wound healing in a subject in need thereof.

Group II: Claims 22-24, directed to a method for regulating a skin condition in a subject in need thereof comprising contacting skin of the subject with a composition.

The group of inventions listed above 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:

*****See supplemental box below*****

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.:
1-21

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
Information on patent family members

International application No.

PCT/US 20/20229

Box III

Group I requires the special technical feature of a method for promoting wound healing in a subject in need thereof comprising contacting a wounded tissue of the subject with a first composition comprising a therapeutic amount of extracellular vesicles (EVs) derived from human amniotic fluid (AF), wherein the therapeutic amount is effective to reduce wound area and to promote repair of the wounded tissue, not required by Groups II.

Group II requires the special technical feature of a method for regulating a skin condition in a subject in need thereof comprising contacting skin of the subject with a composition comprising a therapeutic amount of extracellular vesicles (EVs) derived from human amniotic fluid (AF), wherein the therapeutic amount is effective to improve skin texture, reduce wrinkles, or both, thereby regulating the skin condition, not required by Groups I.

Common technical features:

Groups I-II share the technical feature of a method comprising contacting a tissue of the subject with a composition comprising a therapeutic amount of extracellular vesicles (EVs) derived from human amniotic fluid (AF)

These shared technical features, however, do not provide a contribution over the prior art, as being obvious over US 2016/0184363 A1 to University of Miami (hereinafter UM).

UM discloses a method for promoting wound healing (para [0020] .. In one embodiment, the present invention provides an isolated preparation of microvesicles that promotes or enhances wound healing. In one embodiment, the wound is a full-thickness burn. In one embodiment, the wound is a second-degree burn.. it is well understood the healing is for a patient in need of the healing and the preparation is used in a method of wound healing) comprising contacting a wounded tissue of the subject (para [0322] .. Full thickness wounds were created on the backs of pigs using a 10 mm punch biopsy instrument. Microvesicles were isolated from culture medium conditioned using autologous bone marrow-derived mesenchymal stem cells, either according to the methods described in Example 1 (the conventional ultracentrifugation method), or by the methods described in Example 3. 30 micrograms of microvesicles were administered to the wounds by local injection at the time of wounding and at Days 1 and 2. Controls were treated with saline or allowed to heal air exposed.. the local administration is contacting) with a first composition comprising a therapeutic amount of extracellular vesicles (EVs) derived from human amniotic fluid (AF) (para [0079] .. In one embodiment, the present invention provides reagents and kits to isolate microvesicles from biological fluids according to the methods of the present invention.. para [0080] .. The biological fluid may be peripheral blood, sera, plasma, ascites, urine, cerebrospinal fluid (CSF), sputum, saliva, bone marrow, synovial fluid, aqueous humor, amniotic fluid..). UM does not disclose a specific embodiment wherein vesicles from amniotic fluid are contacted with the wound. It would have been obvious to one skilled in the art to test this specific embodiment using routine experimentation.

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

As the technical features were known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups. Groups I-II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.