(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 January 2007 (04.01.2007)

PCT

(10) International Publication Number
WO 2007/000768 A3

(51) International Patent Classification:
*C07K 14/00* (2006.01) *A61K 38/00* (2006.01)

(21) International Application Number:
PCT/IL2006/000753

(22) International Filing Date: 28 June 2006 (28.06.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/694,438 28 June 2005 (28.06.2005) US
60/696,782 7 July 2005 (07.07.2005) US

(71) Applicant *(for all designated States except US)*: **YEDA RESEARCH AND DEVELOPMENT CO. LTD. AT THE WEIZMANN INSTITUTE OF SCIENCE** [IL/IL]; P.O. Box 95, 76100 Rehovot (IL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **PELES, Elior** [IL/IL]; 56 Carmel Street, 73605 Rehovot (IL). **ESHED, Yael** [IL/IL]; P.O. Box 909, 83109 Moshav Orot (IL).

(74) Agents: **WEBB, Cynthia** et al.; WEBB & ASSOCIATES, P.O. Box 2189, 76121 Rehovot (IL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**
— *with international search report*
— *with sequence listing part of description published separately in electronic form and available upon request from the International Bureau*

(88) Date of publication of the international search report:
9 April 2009

WO 2007/000768 A3

(54) Title: GLIOMEDIN, FRAGMENTS THEREOF AND METHODS OF USING SAME

(57) Abstract: The present invention relates to pharmaceutical compositions comprising gliomedin and active fragments thereof, polynucleotides encoding gliomedin, host cells expressing gliomedin, antibodies to gliomedin and small interfering RNA (siRNA) molecules that down regulate the expression of gliomedin and methods of using same.. The present invention also provides methods of treating and diagnosing neurological disorders using the pharmaceutical compositions and antibodies of the invention.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL06/00753

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **C07K 14/00**( 2006.01);**A61K 38/00**( 2006.01)

USPC: 530/350;514/2
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)
U.S. : 530/350;514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STIC (sequence), EAST, STN (Medline & Biosis)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 2005/0074762 A1 (NAKAMURA et al.) 07 April 2005 (07.04.2005), SEQ ID NO:3, and page 8, [0086]-[0087]. | 1-5, 7 and 8 |

☐ 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

"E" earlier application or patent 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 |
|---|---|
| 23 July 2008 (23.07.2008) | 12 AUG 2008 |
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201 | Authorized officer<br>Dong Jiang<br>Telephone No. 571-272-1600 |

Form PCT/ISA/210 (second sheet) (April 2007)

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL06/00753

## 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:
Please See Continuation 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 any 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.: 1-5,7 and 8

**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.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

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, claim(s) 1-5, 7 and 8, drawn to an isolated polypeptide, a fragment, an analog or a derivative thereof, and a pharmaceutical composition thereof.

Group II, claim(s) 6 and 9-14, drawn to a polynucleotide, a pharmaceutical composition thereof, an expression vector comprising the polynucleotide, and a host cell thereof.

Group III, claim(s) 15-20, drawn to a monoclonal antibody.

Group IV, claim(s) 21-24, drawn to a double stranded siRNA.

Group V, claim(s) 25 in part, 26 and 27, drawn to a method of treatment using the polypeptide.

Group VI, claim(s) 25 in part, 26 and 27, drawn to a method of treatment using the vector comprising the polynucleotide.

Group VII, claim(s) 28-30, drawn to a method of treatment with a host cell.

Group VIII, claim(s) 31-42, drawn to a method of diagnosis with the monoclonal antibody.

Group IX, claim(s) 43-45, drawn to a method of down-regulating gliomedin expression with an siRNA.

The inventions listed as Groups I-IX 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:

This authority considers that the main invention in the instant application comprises the first-recited product, an isolated polypeptide, a fragment, an analog or a derivative thereof, and a pharmaceutical composition thereof. The polypeptide of Group I and the encoding polynucleotide of Group II invention are unrelated, each to each other as either is not itself an advance over the *prior art*. For instance, Nakamura et al. (US 2005/0074762 A1) discloses a nucleic acid (SEQ ID NO:1) and the encoded polypeptide, an adiponectin-associated protein, which amino acid sequence of SEQ ID NO:3 comprises the present SEQ ID NO:18 with 100% sequence identity (see computer printout of the search results). Thus, the Nakamura reference renders the present claim 1, among the other, not novel. As neither the polynucleotide nor the encoded polypeptide is novel, the technical feature of the polypeptide sequence is not special, and the groups do not share a special technical feature, and are not so linked by a single inventive concept under PCT Rule 13.1. Additionally, the other claimed products in groups III and IV are physically and functionally distinct chemical entities, which share neither structure nor function with the polypeptide of Group I, and therefore, are not so linked to the main invention by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single general inventive concept. Further, both Groups I and V all require the technical feature of polypeptide, however as evidenced by Nakamura et al. (see above), the polypeptide does not make a contribution over the prior art. Accordingly, the first method of use (Group V) is not linked to the product used (Group I). Unity is lacking between product (Group I) and the method of use (Group V). The additional methods of groups VI-IX do not correspond to the main invention, as they are neither a method of making,

nor a method of using said nucleic acid. Therefore, they are not considered to share a special technical feature with the main invention within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within the meaning of PCT Rule 13.1.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Three groups of species elections are required:
A. An oligonucleotide selected from:
(1) SEQ ID NO:3; (2) SEQ ID NO:4; and (3) SEQ ID NO:5.

B. A neurological damage selected from:
(1) MS; (2) axonal injury; (3) lack of ion channel in axolemma; (4) disordered axonal clustering of $Na^+$ channels; (5) damaged initial Schwann cell myelination; (6) damaged initial nerve development; and (7) demyelination-associated disease.

C. A diagnostic agent selected from:
(1) radionuclides; (2) ultrasound contrast agents; (3) MRI contrast agents; (4) an dyes; (5) fluorescent compounds; and (6) paramagnetic metals.

The claims are deemed to correspond to the species listed above in the following manner:

Species A(1)-(3): claims 24 and 45.
The following claim(s) are generic: claim 21 is generic for claim 24; and claim 43 is generic for claim 45.

Species B(1)-(7): claim 26.
The following claim(s) are generic: claim 25.

Species C(1)-(6): claim 34.
The following claim(s) are generic: claim 33.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

With respect to group A species election set forth above, each SEQ ID NO set forth above has distinct chemical, and structural properties, and therefore, each does not share a special technical feature with the other within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within themeaning of PCT Rule 13.1.

With respect to group B species election set forth above, the 7 species represent different types of diseases/conditions, and each species has distinct clinical pathology, manifestation and prognosis, and needs different treatment, therefore, these species do not share a special technical feature within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within the meaning of PCT Rule 13.1.

With respect to group C species election set forth above, the 6 species represent different chemical entities, and each has distinct chemical, and structural properties, and therefore, these species do not share a special technical feature within the meaning of PCT Rule 13.2, and thus do not relate to a single invention concept within the meaning of PCT Rule 13.1.