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Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv))

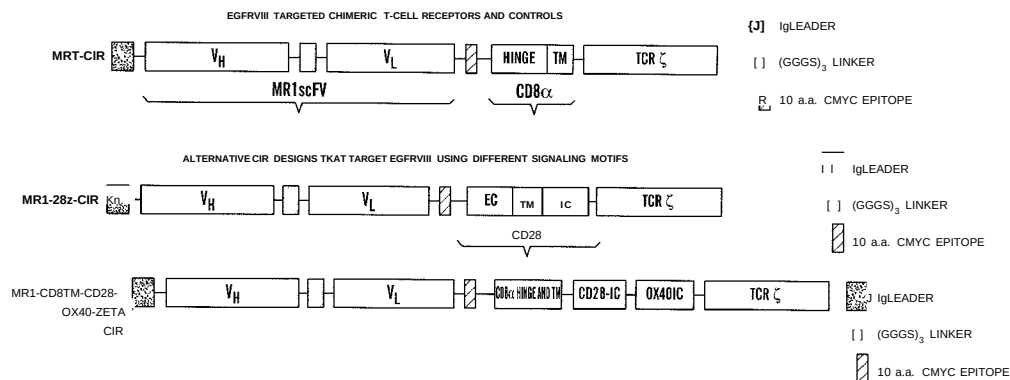
Published:

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments  
— with information concerning authorization of rectification of an obvious mistake under Rule 91.1

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

18 September 2008

(54) Title: CHIMERIC T-CELL RECEPTORS AND T-CELLS TARGETING EGFRVIII ON TUMORS



(57) Abstract: Chimeric T-cell receptor proteins have been produced in cells by the construction of nucleic acids and vectors, and the transfection of the vectors into cells. The chimeric proteins comprise, as an extracellular binding portion, a single chain antibody portion that binds to EGFRvIII, a transmembrane portion derived from human CD8α or CD28, and an intracellular signaling portion derived from human CD3ζ. The invention includes nucleic acids, vectors and cells associated with the production of the chimeric membrane protein, as well as methods to treat tumors bearing EGFRvIII, a mutant epidermal growth factor receptor.

# INTERNATIONAL SEARCH REPORT

International application No

**PCT/US2007/021575**

**A. CLASSIFICATION OF SUBJECT MATTER**

**INV. C07K14/705 C07K16/28 C07K16/30 C07K16/46 A61K39/395**

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)

**C07K**

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 practical search terms used)

**EPO-Internal , BIOSIS, EMBASE, MEDLINE, WPI Data, Sequence Search**

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                         | Relevant to claim No |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| Y          | <b>BULLAIN S S (REPRINT) ET AL: "Chimeric T-cell receptor therapy for glioblastoma multiforme"</b><br>NEUROSURGERY, (AUG 2006) VOL. 59, NO. 2, PP. 486-486. ISSN: 0148-396X. PB - LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA., August 2006 (2006-08), XP009102655<br>the whole document | 1-15                 |
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|            | -/-                                                                                                                                                                                                                                                                                                                        |                      |



Further documents are listed in the continuation of Box C



See patent family annex.

\* Special categories of cited documents :

<sup>1</sup>A' document defining the general state of the art which is not considered to be of particular relevance

<sup>1</sup>E" earlier document but published on or after the international filing date

<sup>1</sup>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)

<sup>1</sup>O' document referring to an oral disclosure, use, exhibition or other means

<sup>1</sup>P' document published prior to the international filing date but later than the priority date claimed

<sup>1</sup>r' 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

<sup>1</sup>< 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

<sup>1</sup>r' 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.

<sup>1</sup>&1 document member of the same patent family

Date of the actual completion of the international search

**4 July 2008**

Date of mailing of the international search report

**15/07/2008**

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/021575

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication where appropriate, of the relevant passages                                                                                                                                                                                                                                                    | Relevant to claim No |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| Y          | US 2002/132983 A1 (JUNGHANS RICHARD P [US]) 19 September 2002 (2002-09-19)<br>the whole document<br>-----                                                                                                                                                                                                                            | 1-15                 |
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| A          | KERSHAW MICHAEL H ET AL: "Supernatural T cells: Genetic modification of T cells for cancer therapy"<br>NATURE REVIEWS IMMUNOLOGY, vol. 5, no. 12, December 2005 (2005-12), pages 928-940, XP009102639<br>ISSN: 1474-1733<br>-----                                                                                                    |                      |

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/021575

## 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. ☒ IX I Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

**Although claims 13-15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**

### 2. ☒ J I 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:

1. ☐ I As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable ☒ I aaiimss.

2. ☐ I As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ I 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. ☒ D 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.:

### 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/US2007/021575

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date         |
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