Abstract:

Title: TARGETED PROTEIN SILENCING USING CHIMERICAS BETWEEN ANTIBODIES AND UBIQUITINATION ENZYMES

The present invention relates to an isolated chimeric molecule comprising a degradation domain including a eukaryotic U-box motif and a targeting domain capable of immunospecifically directing the degradation domain to a substrate where the targeting domain is heterologous to the degradation domain. A linker couples the degradation domain to the targeting domain. Also disclosed are compositions as well as methods of treating a disease, substrate silencing, screening agents for therapeutic efficacy against a disease, and methods of screening for disease biomarkers.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
   C07K 19/00(2006.01)i, C12N 9/00(2006.01)i, C07K 16/00(2006.01)i, A61K 35/12(2006.01)i

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 19/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
   Korean utility models and applications for utility models
   Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
   eKOMPASS(KIPO internal), PubMed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
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<tbody>
<tr>
<td>Y</td>
<td>NISSIM, A. et al. 'Methods for targeting biologicals to specific disease sites' Trends in Molecular Medicine. Vol. 10(6), pp. 269-274 (June 2004) See abstract and Fig. 2.</td>
<td>1-17, 21-35</td>
</tr>
</tbody>
</table>

* 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 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

23 OCTOBER 2012 (23.10.2012)

Date of mailing of the international search report

24 OCTOBER 2012 (24.10.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan City, 302-701, Republic of Korea
Facsimile No. 82-42-472-7140

Authorized officer
KIM, JI YUN
Telephone No. 82-42-481-8288

Form PCT/ISA/210 (second sheet) (July 2009)
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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### Box No. II  Observations where certain claims were found unsearable (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.: 18-20**  
   because they relate to subject matter not required to be searched by this Authority, namely:  
   Said claims pertain to methods for treatment of the human body, thus relate to a subject-matter which International Searching Authority is not required to search under PCT Art. 17(2)(a)(i) and Rule 39.1(iv).

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:

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 an additional fee, this Authority did not invite payment of any additional fee.**

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.:**

### 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.
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
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