Title: COMPOSITIONS AND METHODS FOR TREATING CANCER USING IMMUNOCONJUGATES AND CHEMOTHERAPEUTIC AGENTS

Abstract: The present invention is based on the discovery that the administration of at least one immunoconjugate and at least one chemotherapeutic agent provides an unexpectedly superior treatment for cancer. The present invention is directed to compositions comprising at least one immunoconjugate and at least one chemotherapeutic agent and to methods of treating cancer using at least one immunoconjugate and at least one chemotherapeutic agent. The present invention also provides methods of modulating the growth of selected cell populations, such as cancer cells, by administering a therapeutically effective amount of at least one chemotherapeutic agent and at least one immunoconjugate.
A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 59/505; C07K 16/00
US CL. : 426/180.1, 178.1; 850/387.1

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. : 426/180.1, 178.1; 850/387.1

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)

DIALOG, WEST

search terms: chemotherapeutic agents, immunoconjugate, anti-mitotic agents, cancer.

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>
</thead>
</table>

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

Date of the actual completion of the international search

22 MARCH 2001

Date of mailing of the international search report

01 MAY 2001

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks

Box PCT
Washington, D.C. 20231

Authorized officer

MINH-TAM DAVIS

Facsimile No. (703) 505-5950

Telephone No. (703) 505-0196

Form PCT/ISA/910 (second sheet) (July 1998)*
### 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>
</thead>
</table>
### INTERNATIONAL SEARCH REPORT

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(4)(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(e).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

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 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.:

1-19, 40-61

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)
BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single 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, claim(s) 39, 40, 41, drawn to 1) a method of treating cancer, comprising administering a chemotherapeutic agent, and one immunoconjugate, wherein the immunoconjugate comprises one cell binding agent and an anti-mitotic agent, and 2) a composition comprising a chemotherapeutic agent, and one immunoconjugate, wherein the immunoconjugate comprises one cell binding agent and an anti-mitotic agent.

Group II, claims 55-59, drawn to a method for modulating growth, comprising administering a chemotherapeutic agent, and one immunoconjugate, wherein the immunoconjugate comprises one cell binding agent and an anti-mitotic agent.

Group III, claims 60-65, drawn to a method of treating autoimmune disease, a graft rejection, a viral infection or a parasite infection, comprising administering a chemotherapeutic agent, and one immunoconjugate, wherein the immunoconjugate comprises one cell binding agent and an anti-mitotic agent.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 15.8, they lack the same or corresponding special technical features for the following reasons:

An international stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. If multiple products, processeses of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(b)(a) and 1.475(c), 87 C.F.R. 1.475(d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 87 CFR 1.475(d)).

Group I, drawn to 1) a method of treating cancer, comprising administering a chemotherapeutic agent, and one immunoconjugate, and a composition comprising a chemotherapeutic agent, and one immunoconjugate, form a single inventive concept.

Group II is an additional method, drawn to a method of modulating the growth of cells, which could be in vitro methods, and thus different from the in vivo methods of group I. Further, modulation of tumor cell growth does not necessarily mean that cancer is treated.

Group III is an additional method, drawn to a method of treating autoimmune disease, a graft rejection, a viral infection or a parasite infection, which is distinct from the method of group I, because autoimmune disease, a graft rejection, a viral infection or a parasite infection are different diseases with different etiology.