Title: USE OF IL-21 IN CANCER AND OTHER THERAPEUTIC APPLICATIONS

Abstract: Methods for treating mammals with cancer and infections using molecules that have an IL-21 functional activity are described. The molecules having IL-21 functional activities include polypeptides that have homology to the human IL-21 polypeptide sequence and proteins fused to a polypeptide with IL-21 functional activity. The molecules can be used as a monotherapy or in combination with other known cancer or viral therapeutics.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00, 38/20, 38/21, 39/00
US CL : 424/85.1, 85.2, 185.1, 192.1

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. : 424/85.1, 85.2, 185.1, 192.1

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)
WEST search for IL-21.

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>

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

Date of the actual completion of the international search
17 September 2004 (17.09.2004)

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Date of mailing of the international search report
07 OCT 2004

Authorized officer
Jegathesan Scharasevan
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Form PCT/ISA/210 (second sheet) (July 1998)
### 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(2)(a) for the following reasons:

1. **Claim Nos.:**
   - because they relate to subject matter not required to be searched by this Authority, namely:

2. **Claim 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. **Claim Nos.:**
   - because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### 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 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 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.: 1-9

**Remark on Protest**

| ☐ | The additional search fees were accompanied by the applicant's protest. |
| ☐ | No protest accompanied the payment of additional search fees. |
BOX II. 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) 1-9, drawn to a method of treating Non-Hodgkins lymphoma and other cancers by administering to a subject in need thereof a therapeutically effective amount of a polypeptide having a functional activity of IL-21.

Group II, claim(s) 10-18, drawn to a method of treating Non-Hodgkins lymphoma and other cancers by administering to a subject in need thereof a therapeutically effective amount of a fusion polypeptide having a functional activity of IL-21.

Group III, claim(s) 19-24, drawn to a method of treating a viral infection by administering to a subject in need thereof a therapeutically effective amount of a polypeptide having a functional activity of IL-21.

Group IV, claim(s) 25-27, drawn to a method of treating a viral infection by administering to a subject in need thereof a therapeutically effective amount of a fusion polypeptide having a functional activity of IL-21.

Group V, claim(s) 28-32, drawn to a method of treating a bacterial infection by administering to a subject in need thereof a therapeutically effective amount of a polypeptide having a functional activity of IL-21.

Group VI, claim(s) 33-37, drawn to a method of treating a bacterial infection by administering to a subject in need thereof a therapeutically effective amount of a fusion polypeptide having a functional activity of IL-21.

The inventions listed as Groups I-VI 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: Claims 1-9 at least are anticipated by Novak et al. (U. S. Patent No: 6, 307, 024). Consequently, the special technical feature, which links Groups I-II, does not provide contribution over the prior art, so the unity of invention is lacking. Inventions, I-VI are different from each other as they are directed to non equivalent methods.

The claims of these groups are directed to different inventions, which are not linked to form a single general inventive concept under PCT Rule 13.1. The claims in the different groups lack the same or corresponding special technical features. In particular, each group is directed to different methods. Accordingly, the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept and lack of unity is deemed proper.