Title: STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

Abstract: Novisprin peptides are antimicrobial agents with potent activity against Gram-negative bacteria. The peptides are nonhemolytic, exhibit reduced in vitro cytotoxicity relative to other antimicrobial peptides, and were well-tolerated in vivo after intravenous injection. Novisprins also bind lipopolysaccharide (LPS), a property that may mitigate symptoms associated with Gram-negative bacterial infection. A pharmaceutical composition comprising novisprin as an active agent is administered to a patient suffering from or predisposed to a microbial infection, particularly Gram-negative bacterial infections.
### INTERNATIONAL SEARCH REPORT

**Classification of Subject Matter**
- IPC: A61K 38/00, 38/00; C07K 5/00, 16/00, 17/00
- US Cl: 580/300, 396; 514/2

According to International Patent Classification (IPC) or to both national classification and IPC.

### Fields Searched

Minimum documentation searched (classification system followed by classification symbols)
- U.S.: 580/300, 396; 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)
- Database: registry, caplus, biosis, medline, embase, wpids, confici, aseansearch, jicst-eplus, japi

### 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>
<tbody>
<tr>
<td>X,P</td>
<td>WO 01/12668 A1 (UNIVERSITY OF IOWA RESEARCH FOUNDATION) 22 February 2001, truncated peptides based upon SMAP29 and RCAP18, method inhibiting microbial growth by administering the peptide, see abstract; SEQ ID NO: 17, see page 3 and claims.</td>
<td>1-2, 4-8, 10-19, 21-27</td>
</tr>
<tr>
<td>X,E</td>
<td>Database: A Geneseq 032802; Accession NO: AAB70648; TACK et al. &quot;Ovine SMAP 29 cathelicidin derived antimicrobial peptide SEQ ID NO: 1;&quot; 15 May 2001; having 89.1% sequence identity to SEQ ID NO: 17; see entire document.</td>
<td>1-2, 4-8, 10-19, 21-27</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C.

See patent family annex.

**Date of the actual completion of the international search:**
- O6 MAY 2003

**Date of mailing of the international search report:**
- 21 MAY 2003

**Name and mailing address of the ISA/US Commissioner of Patents and Trademarks**
- Box PCT
- Washington, D.C. 20231

**Facsimile No.**
- (703) 505-3990

**Form PCT/ISA/210 (second sheet) (July 1998)***
<table>
<thead>
<tr>
<th>Category</th>
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</thead>
<tbody>
<tr>
<td>X</td>
<td>MAHONEY et al. Molecular analysis of the sheep cathelin family reveals a novel antimicrobial peptide. FEBS Letters. 1995, Vol. 377, pages 519-522, A prepropeptide bacterial agent (see abstract); antimicrobial activity (see page 519, col 2, paragraph 2.4, Table 1 and Figure 4)</td>
<td>1-2, 4-8, 10-17</td>
</tr>
<tr>
<td>X</td>
<td>Database: PIR_71; Accession NO: S68411; MAHONEY et al. &quot;Cathelin-related protein 2 precursor-sheep (fragment)&quot;. 28 October 1996; having 53.3% sequence identity to SEQ ID NO: 17; see entire document.</td>
<td>1-2, 4-8, 10-17</td>
</tr>
</tbody>
</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(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 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, 2, 4-8, 10-19, 21-27 all in part, and SEQ ID NO: 17

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 WAS LACKING
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.

Groups 1-55. Claims 1, 2, 4-8, 10-19, 21-27, directed to an antimicrobial polypeptide comprising the sequence as set forth in SEQ ID NO: 1, KNLRRX1X2RXX5X4HIIKXYG wherein X1, X2, X3 and X4 are selected from the group of glycine, threonine, serine, and isoleucine with the provision that no more than 3 of the X residues are isoleucine, wherein said peptide comprises the amino acid sequence set forth in any one of SEQ ID NO: 3 to SEQ ID NO: 37; an antimicrobial formulation comprising the said peptides,a method for treating a microbial infection using the said peptides.

If a Group is elected, only one SEQ ID NO. to be selected and X1, X2, X3, X4 values to be defined in claims 1, 2, 7, 8, 18 and 19.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups 1-55 do not relate to a single 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:

The protein of SEQ ID NO: 3-37, each invention are unrelated, each to the other. The antimicrobial polypeptide sequences of said SEQ ID NO.s are structurally distinct proteins and do not share a special technical feature. Furthermore, the technical feature that links the protein, methods using the proteins is not a contribution over the prior art. See the various documents cited in the search report. Thus the technical feature of the protein sequences is not special and the groups are not so linked under PCT Rule 13.1.