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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

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(54) Title: **LIVE MICROBIAL MICROBICIDES**

(57) Abstract: The present invention relates, e.g. to a commensal bacterium which can colonize the genitourinary and/or gastrointestinal mucosa, and which, under suitable conditions, secretes a heterologous antimicrobial polypeptide, wherein the secreted antimicrobial polypeptide is effective to inhibit infectivity by, or a pathogenic activity of, a pathogen. In a most preferred embodiment, the antimicrobial polypeptide inhibits HIV infection (e.g., fusion) and/or pathogenesis. Also described are preventive or therapeutic compositions comprising the commensal bacteria, and methods to inhibit infectivity and/or pathogenesis, using the bacteria.



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A. CLASSIFICATION OF SUBJECT MATTER A61K35/74 A61K38/16 C07K14/16 C12N15/69				
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) A61K C07K C12N				
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, WPI Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
P,X	RAO SRINIVAS ET AL: "Toward a live microbial microbicide for HIV: commensal bacteria secreting an HIV fusion inhibitor peptide." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 23 AUG 2005, vol. 102, no. 34, 23 August 2005 (2005-08-23), pages 11993-11998, XP002371507 ISSN: 0027-8424 the whole document	1-35		
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.				
* Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; border: none;"> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document 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 another 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 </td> <td style="width: 50%; vertical-align: top; border: none;"> "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 </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document 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 another 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
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document 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 another 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			
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/228297 A1 (CHANG CHIA-HWA ET AL) 11 December 2003 (2003-12-11)	1,10-14, 18,20, 23,25, 32-34
Y	the whole document	2-9, 15-17, 19,21, 22,24, 26-31,35
X	CHANG THERESA L-Y ET AL: "Inhibition of HIV infectivity by a natural human isolate of Lactobacillus jensenii engineered to express functional two-domain CD4." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 30 SEP 2003, vol. 100, no. 20, 30 September 2003 (2003-09-30), pages 11672-11677, XP002371508 ISSN: 0027-8424	1,10-14, 18,20, 23,25, 32-34
Y	the whole document	2-9, 15-17, 19,21, 22,24, 26-31,35
Y	GIOMARELLI BARBARA ET AL: "The microbicide cyanovirin-N expressed on the surface of commensal bacterium Streptococcus gordonii captures HIV-1." AIDS (LONDON, ENGLAND) 5 JUL 2002, vol. 16, no. 10, 5 July 2002 (2002-07-05), pages 1351-1356, XP002371509 ISSN: 0269-9370 the whole document	1-35
Y	BENINATI C ET AL: "Therapy of mucosal candidiasis by expression of an anti-idiotypic in human commensal bacteria" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 18, no. 10, October 2000 (2000-10), pages 1060-1064, XP002261610 ISSN: 1087-0156 the whole document	1-35

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KRUGER C ET AL: "In situ delivery of passive immunity by lactobacilli producing single-chain antibodies" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 20, no. 7, July 2002 (2002-07), pages 702-706, XP002321895 ISSN: 1087-0156 the whole document	1-35
A	KRUIS W ET AL: "Maintaining remission of ulcerative colitis with the probiotic Escherichia coli Nissle 1917 is as effective as with standard mesalazine." GUT. NOV 2004, vol. 53, no. 11, November 2004 (2004-11), pages 1617-1623, XP002371510 ISSN: 0017-5749	
A	REMBACKEN B ET AL: "Non-pathogenic Escherichia coli versus mesalazine for the treatment of ulcerative colitis: a randomised trial" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 354, no. 9179, 21 August 1999 (1999-08-21), pages 635-639, XP004831404 ISSN: 0140-6736	
A	TROMM A ET AL: "The probiotic E. coli strain Nissle 1917 for the treatment of collagenous colitis: first results of an open-label trial." ZEITSCHRIFT FÜR GASTROENTEROLOGIE. MAY 2004, vol. 42, no. 5, May 2004 (2004-05), pages 365-369, XP009063168 ISSN: 0044-2771	
A	TZSCHASCHEL B D ET AL: "AN ESCHERICHIA COLI HEMOLYSIN TRANSPORT SYSTEM-BASED VECTOR FOR THEEXPORT OF POLYPEPTIDES: EXPORT OF SHIGA-LIKE TOXIN IIEB SUBUNIT BY SALMONELLA TYPHIMURIUM AROA" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 14, June 1996 (1996-06), pages 765-769, XP002060319 ISSN: 1087-0156	
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/030216

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FERNÁNDEZ L A ET AL: "Specific secretion of active single-chain Fv antibodies into the supernatants of Escherichia coli cultures by use of the hemolysin system." APPLIED AND ENVIRONMENTAL MICROBIOLOGY. NOV 2000, vol. 66, no. 11, November 2000 (2000-11), pages 5024-5029, XP002371602 ISSN: 0099-2240	
A	ECKERT D M ET AL: "MECHANISMS OF VIRAL MEMBRANE FUSION AND ITS INHIBITION" ANNUAL REVIEW OF BIOCHEMISTRY, PALTO ALTO, CA, US, vol. 70, 2001, pages 777-810, XP001152929 ISSN: 0066-4154	

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Box 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. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 25-33 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. ☐ 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 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.
- ☐ No protest accompanied the payment of additional search fees.

Information on patent family members

PCT/US2005/030216

Patent document
cited in search report

Publication
date

Patent family member(s)

Publication
date

US 2003228297	A1	11-12-2003	NONE
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