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*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: COMPOSITIONS AND METHODS RELATING TO THE DAPTOMYCIN BIOSYNTHETIC GENE CLUSTER

(57) Abstract: The invention provides nucleic acid molecules comprising all or a part of a daptomycin biosynthetic gene cluster. The daptomycin biosynthetic gene cluster may be derived from *Streptomyces*, preferably from *S. roseosporus*. The invention also provides other nucleic acid molecules from *S. roseosporus*. The invention further provides polypeptides encoded by the nucleic acid molecules, antibodies that specifically bind to the polypeptides, and methods of using the nucleic acid molecules, polypeptides and antibodies to produce daptomycin and other compounds.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/24310

A. CLASSIFICATION OF SUBJECT MATTER		
IPC(7) : C07H 21/04; C12N 15/74, 1/20, 1/14, 1/16, 5/00, 5/02, 5/04, 5/10, 1/00; C12P 21/06; C12Q 1/68		
US CL : 536/23.1, 23.2, 23.7; 435/320.1, 252.3, 254.11, 419, 325, 183, 69.1, 6		
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. : 536/23.1, 23.2, 23.7; 435/320.1, 252.3, 254.11, 419, 325, 183, 69.1, 6		
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) STN, search terms: daptomycin, polyketide synthase, roseosporus		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MCHENNEY M.A. et al. Molecular Cloning and Physical Mapping of the Daptomycin Gene Cluster from Streptomyces roseosporus. J. Bacteriol. January 1998, Vol. 180, No. 1, pages 143-151.	1, 4
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Y		
A	MCHENNEY. M.A. et al. Gene transfer and transposition mutagenesis in Streptomyces roseosporus: mapping of insertions that influence daptomycin or pigment production. Microbiology. September 1996, Vol. 142, pages 2363-2373.	1, 4, 55-73
A	MOOTZ. H.D. et al. Design and application of multimodular peptide synthetases. Current Opinion in Biotechnology. 1999, Vol. 10, No. 4, pages 341-348.	55-73
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"B"	earlier application or patent published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
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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 and 4, drawn to nucleic acid molecules, vectors, and host cells.

Group II, claim(s) 55-68 and 71-73, drawn to methods for producing a hybrid lipopeptide or peptide core thereof comprising a portion of a daptomycin lipopeptide or peptide core.

Group III, claim(s) 69, drawn to host cells containing hybrid daptomycin-NRPS gene clusters.

Group IV, claim(s) 70, drawn to hybrid lipopeptides or peptide cores comprising a portion of a daptomycin lipopeptide or peptide core.

The inventions listed as Groups I-IV 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: a technical feature throughout the claims is a daptomycin gene cluster. This technical feature is not a special technical feature because daptomycin gene clusters were known in the prior art prior at Applicants' invention.

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 2,3,5-21,28-36 and 38-54
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:
Claims 2, 3, 5-21, 28-36, and 38-54 are unsearchable because no meaningful search can be carried out in the absence of a computer readable form of the sequence listing. The SEQ ID NOs in the claims cannot be searched.

3. Claim Nos.: 22-27 and 30-37
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.:

Remark on Protest

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

No protest accompanied the payment of additional search fees.