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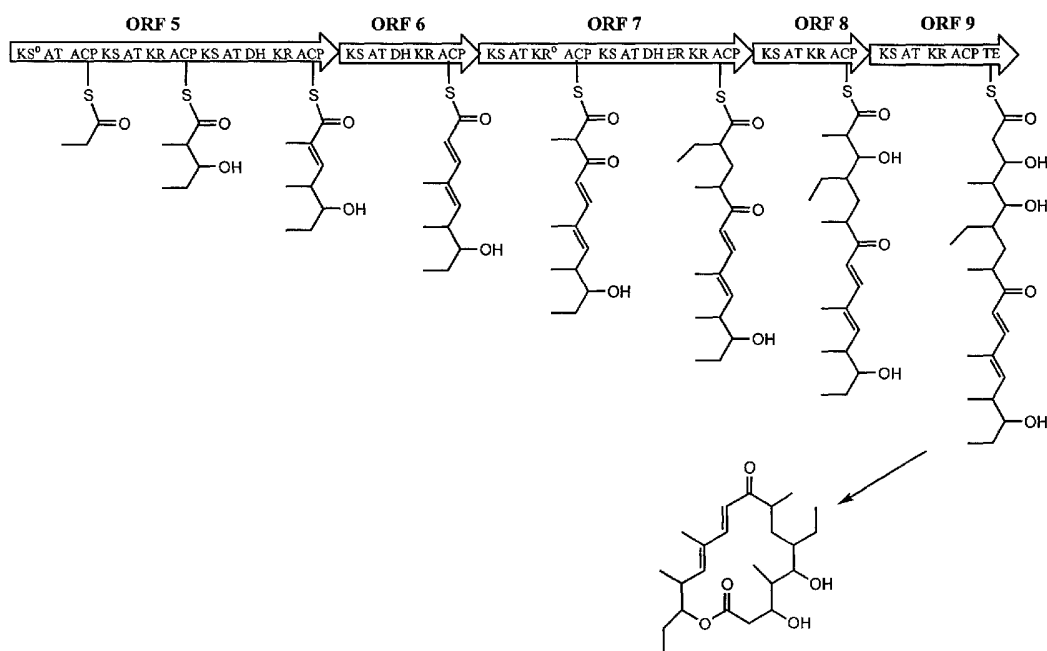
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Saint-Laurent, Québec H4L 5M5 (CA). **YANG, Xianshu** [CA/US]; 39 Trowbridge Street, Belmont, MA 02478 (US).
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[Continued on next page]

(54) Title: GENES AND PROTEINS FOR THE BIOSYNTHESIS OF ROSARAMICIN



(57) Abstract: Genes and proteins involved in the biosynthesis of macrolides by microorganisms, in particular the nucleic acids forming the biosynthetic locus for the 16-member macrolide rosaramicin from *Micromonospora carbonacea*. These nucleic acids can be used to make expression constructs and transformed host cells for the production of rosaramicin. The genes and proteins allow direct manipulation of macrolides and related chemical structures via chemical engineering of the proteins involved in the biosynthesis of rosaramicin.

**Declarations under Rule 4.17:**

- as to the identity of the inventor (Rule 4.17(i)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

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Inte nal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/52 C12P19/62 C12N9/00 C12N15/63

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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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, BIOSIS, MEDLINE, EMBASE, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! Entry SF08223, 20 April 1994 (1994-04-20) MERSON-DAVIES L.A. ET AL.: "Streptomyces fradiae cytochrome P-450, dTDP-glucose synthase, dTDP-glucose dehydratase, thioesterase, Ty1CVI (ty1CVI), and Ty1R (ty1R) genes " Database accession no. U08223 XP002228882 the whole document & MERSON-DAVIES L.A. ET AL.: "Analysis of five tylosin biosynthetic genes from the ty1IBA region of the Streptomyces fradiae genome" MOLECULAR MICROBIOLOGY, vol. 13, 1994, pages 349-355, --- -/--</p>	1-3, 18, 19

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 02/01177

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! Entry SFTYLDRF, 8 January 1997 (1997-01-08) GANDECHA A.R. : "Streptomyces fradiae tyIMIII(orf1*), tyIMII(orf2*), tyIMI(orf3*) and ccr(orf4*) genes" Database accession no. X81885 XP002228883 the whole document</p> <p style="text-align: center;">---</p>	1-3, 18, 19
X	<p>DATABASE SWALL 'Online! Entry Q9ZBK1, 1 May 1999 (1999-05-01) SEEGER, K.J. ET AL.: "Crotonyl CoA reductase" Database accession no. Q9ZBK1 XP002228884 the whole document & BENTLEY, S.D. ET AL.: "A set of ordered cosmids and a detailed genetic and physical map for the 8 Mb Streptomyces coelicolor A3(2) chromosome" MOLECULAR MICROBIOLOGY, vol. 21, 1996, pages 77-96,</p> <p style="text-align: center;">---</p>	13
A	<p>US 4 234 690 A (MARVIN J. WEINSTEIN ET AL.) 18 November 1980 (1980-11-18) column 1, line 31 -column 6, line 29; examples 1-4</p> <p style="text-align: center;">-----</p>	1-25

INTERNATIONAL SEARCH REPORT
Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4234690	A	NONE	