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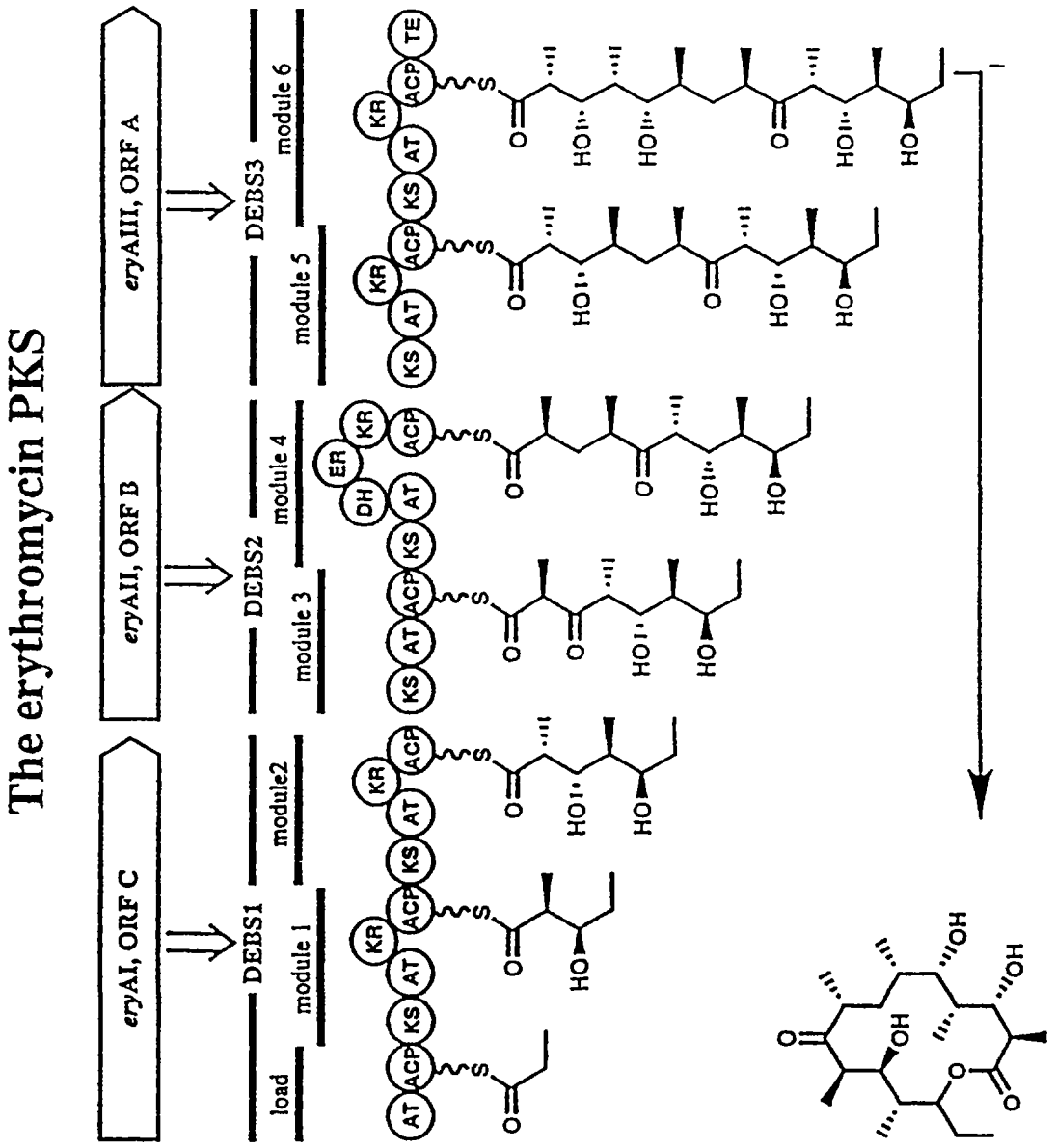


Fig. 1

```
KCLFDAU          ----------------------------MVTGLGIVAPNGLGVGAIWDAVLNGRNGIGPLR
KCLFPEU          MTGTAARTASSQLHASPAGRRGLRGRAVVTGLGIVAPNGLGVGAYWDAVLNGRNGIGPLR
KCLFACT          -------------------------MSVLITGVGVVAPNGLGLAPYWSAVLDGRHGLGPVT
KCLFHIR          -------------------------MSIWVTGMGVVAPNGLGADDHWAATLKGRHGISRLS
KCLFGRA          ------------------MSTPDRRRAVVTGLSVAAPGGLGTERYWKSLLTGENGIAELS
KCLFNOG          ----------------------MTAAVVVTGLGVVAPTGLGVREHWSSTVRGASAIGPVT
KCLFTCM          --------------------MSAPAPVVVTGLGIVAPNGTGTEEYWAATLAGKSGIDVIQ
KCLFCIN          ----------------------MTP-VAVTGMGIAAPNGLGRPTTGRPPWAPRAASAAST
KCLFVNZ          ----------------------MSASVVVTGLGVAAPNGLGREDFWASTLGGKSGIGPLT
KCLFWHIE         -----------MSGPQRTGTGGGSRRAVVTGLGVLSPHGTGVEAHWKAVADGTSSLGPVT
KSGRA            ----------------------MTRRVVITGVGVRAPGGSGTKEFWDLLTAGRTATRPIS
KSHIR            ----------------------MTRRVVITGVGVRAPGGLGAKNFWELLTSGRTATRRIS
KSACT            ----------------------MKRRVVITGVGVRAPGGNGTRQFWELLTSGRTATRRIS
KSCIN            ---------------------MTQRRVAITGIEVLAPGGLGRKEFWQLLSEGRTATRGIT
KSVNZ            ---------------------MTARRVVITGIEVLAPGGTGSKAFWNLLSEGRTATRGIT
KSNOG            -----------------MKESINRRVVITGIGIVAPDATGVKPFWDLLTAGRTATRTIT
KSTCM            -----------------MTRHAEKRVVITGIGVRAPGGAGTAAFWDLLTAGRTATRTIS
KSDAU            ----------------------MNRRVVITGMGVVAPGAIGIKSFWELLLSGTTATRAIT
KSPEU            ----------------------MNRRIVITGIGVVAPGAVGTKPFWELLLSGTTATRAIS
KSWHI            ----------------------MTRRRVAVTGIGVVAPGGIGTPQFWRLLSEGRTATRRIS
                                          :**: : :* . *             .

KCLFDAU          RFADDGRLGRLAGEVSDFVP-EDHLPKRLLVQTDPMTQMTALAAAEWALREAGCAPSS--
KCLFPEU          RFTGDGRLGRLAGEVSDFVP-EDHLPKRLLAQTDPMTQY-ALAAAEWALRESGCSPSS--
KCLFACT          RFDVSRYPATLAGQIDDFHA-PDHIPGRLLPQTDPSTRL-ALTAADWALQDAKADPES-L
KCLFHIR          RFDPTGYPAELAGQVLDFDA-TEHLPKRLLPQTDVSTRF-ALAAAAWALADAEVDPAE-L
KCLFGRA          RFDASRYPSRLAGQIDDFEA-SEHLPSRLLPQTDVSTRY-ALAAADWALADAGVGPESGL
KCLFNOG          RFDAGRYPSKLAGEVPGFVP-EDHLPSRLMPQTDHMTRL-ALVAADWAFQDAAVDPSK-L
KCLFTCM          RFDPHGYPVRVGGEVLAFDA-AAHLPGRLLPQTDRMTQH-ALVAAEWALADAGLEPEK-Q
KCLFCIN          RFDPSGYPAQLAGEIPGFRA-AEHLPGRLVPQTDRVTRL-SLAAADWALADAGVEVAA-F
KCLFVNZ          RFDPTGYPARLAGEVPGFAA-EEHLPSRLLPQTDRMTRL-ALVAADWALADAGVRPEE-Q
KCLFWHIE         REGCAHLPLRVAGEVHGFDA-AETVEDRFLVQTDRFTHF-ALSATQHALADARFGRADVD
KSGRA            FFDASPFRSRIAGEI-DFDAVAEGFSPREVRRMDRATQF-AVACTRDALADSGLDTGA-L
KSHIR            FFDPTPNRSQIAAEC-DFDPEHEGLSPREIRRMDRAAQF-AVVCTRDAVADSGLEFEQ-V
KSACT            FFDPSPYRSQVAAEA-DFDPVAEGFGPRELDRMDRASQF-AVACAREAFAASGLDPDT-L
KSCIN            FFDPAPFRSKVAAEA-DFCGLENGLSPQEVRRMDRAAQF-AVVTAR-AVEDSGAELAA-H
KSVNZ            FFDPTPFRSRVAAEI-DFDPEAHGLSPQEIRRMDRAAQF-AVVAAR-AVADSGIDLAA-H
KSNOG            AFDPSPFRSRIAAEC-DFDPLAEGLTPQQIRRMDRATQF-AVVSARESLEDSGLDLGA-L
KSTCM            LFDAAPYRSRIAGEI-DFDPIGEGLSPRQASTYDRATQL-AVVCAREALKDSGLDPAA-V
KSDAU            TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAGQF-ALVAGQEALTDSGLRIGE-D
KSPEU            TFDATPFRSRIAAEC-DFDPVAAGLSAEQARRLDRAGQF-ALVAGQEALADSGLRIDE-D
KSWHI            LFDPSGLRSQIAAEC-DFEPSDHGLGLATAQRCDRYVQF-ALVAASEAVRDANLDMNR-E
                           :..:   *      .       *   :  ::     :.  :
```

Fig 2A

```
KCLFDAU         -PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
KCLFPEU         -PLEAGVITASASGGFAFGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
KCLFACT         TDYDMGVVTANACGGFDFTHREFRKLWSEG-----PKSVSVYESFAWFY-AVNTGQISIR
KCLFHIR         PEYGTGVITSNATGGFEFTHREFRKLWAQG-----PEFVSVYESFAWFY-AVNTGQISIR
KCLFGRA         DDYDLGVVTSTAQGGFDFTHREFHKLWSQG-----PAYVSVYESFAWFY-AVNTGQISIR
KCLFNOG         PEYGVGVVTASSAGGFEFGHRELQNLWSLG-----PQYVSAYQSFAWFY-AVNTGQVSIR
KCLFTCM         DEYGLGVLTAAGAGGFEFGQREMQKLWGTG-----PERVSAYQSFAWFY-AVNTGQISIR
KCLFCIN         DPLDMGVVTASHAGGFEFGQDELQKLLGQG-----QPVLSAYQSFAWFY-AVNSGQISIR
KCLFVNZ         DDFDMGVVTASASGGFEFGQGELQKLWSQG-----SQYVSAYQSFAWFY-AVNSGQISIR
KCLFWHIE        SPYSVGVVTAAGSGGGEFGQRELQNLWGHG-----SRHVGPYQSIAWFY-AASTGQVSIR
KSGRA           DPSRIGVALGSAVASATSLENEYLVMSDSGREWLVDPAHLSPMMFDYLSPGVMPAEVAWA
KSHIR           PPERIGVSLGSAVAAATSLEQEYLVLSDGGREWQVDPAYLSAHMFDYLSPGVMPAEVAWT
KSACT           DPARVGVSLGSAVAAATSLEREYLLLSDSGRDWEVDAAWLSRHMFDYLVPSVMPAEVAWA
KSCIN           PPHRIGVVVGSAVGATMGLDNEYRVVSDGGRLDLVDHRYAVPHLYNYLVPSSFAAEVAWA
KSVNZ           DPYRVGVTVGSAVGATMGLDEEYRVVSDGGRLDLVDHAYAVPHLYDYMVPSSFSAEVAWA
KSNOG           DASRTGVVVGSAVGCTTSLEEEYAVVSDSGRNWLVDDGYAVPHLFDYFVPSSIAAEVAHD
KSTCM           NPERIGVSIGTAVGCTTGLDREYARVSEGGSRWLVDHTLAVEQLFDYFVPTSICREVAWE
KSDAU           SAHRVGVCVGTAVGCTQKLESEYVALSAGGANWVVDPHRGAPELYDYFVPSSLAAEVAWL
KSPEU           SAHRVGVCVGTAVGCTQKLESEYVALSAGGAHWVVDPGRGSPELYDYFVPSSLAAEVAWL
KSWHI           DPWRAGATLGTAVGGTTRLEHDYVLVSERGSRWDVDDRRSEPHLERAFTPATLSSAVAEE
                     *.  .  .    . :  :  *                :       ::

                                  ↓
KCLFDAU         -HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAMDSSLCP-YGMAAQVRSG
KCLFPEU         -HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAVDSSLCP-YGMAAQVKSG
KCLFACT         -HGMRGPSSALVAEQAGGLDALGHAR-RTIRRGTP-LVVSGGVDSALDP-WGWVSQIASG
KCLFHIR         -HGLRGPGSVLVAEQAGGLDAVGHGG--AVRNGTP-MVVTGGVDSSFDP-WGWVSHVSSG
KCLFGRA         -NIMRGPSAALVGEQAGGLDAIGHAR-RTVRRGPG-WCSAVASTRRSTR-GASSSQLSGG
KCLFNOG         -HGLRGPGGVLVTEQAGGLDALGQAR-RQLRRGLP-MVVAGAVDGSPCP-WGWVAQLSSG
KCLFTCM         -HGMRGHSSVFVTEQAGGLDAAAHAA-RLLRKGTLNTALTGGCEASLCP-WGLVAQIPSG
KCLFCIN         -HGMKGPSGVVVSDQAGGLDALAQAR-RLVRKGTP-LIVCGAVEPRSAPGAGSPSSPAGG
KCLFVNZ         -NGMKGPSGVVVSDQAGGLDAVAQAR-RQIRKGTR-LIVSGGVDASLCP-WGWVAHVASD
KCLFWHIE        -NDFKGPCGVVAADEAGGLDALAHAA-LAVRNGTD-TVVCGATEAPLAP-YSIVCQLGYP
KSGRA           -AGAEGPVIMVSDGCTSGLDSVGYAV-QGTREGSADVVVAGAADTPVSPIVVACFDAIKA
KSHIR           -VGAEGPVAMVSDGCTSGLDSLSHAC-SLIAEGTTDVMVAGAADTPITPIVVSCFDAIKA
KSACT           -VGAEGPVIMVSTGCTSGLDSVGNAV-RAIEEGSADVMFAGAADTPITPIVVACFDAIRA
KSCIN           -VGAEGPSTVVSTGCTSGIDAVGIAV-ELVREGSVDVMVAGAVDAPISPIP-CVLDAIKA
KSVNZ           -VGAEGPNTVVSTGCTSGLDSVGYARGELIREGSADVMIAGSSDAPISPITMACFDAIKA
KSNOG           RIGAEGPVSLVSTGCTSGLDAVGRAA-DLIAEGAADVMLAGATEAPISPITVACFDAIKA
KSTCM           -AGAEGPVTVVSTGCTSGLDAVGYGT-ELIRDGRADVVVCGATDAPISPITVACFDAIKA
KSDAU           -AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDVMLAGGVDAPIAPITVACFDAIRV
KSPEU           -AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDAMVAGGVDAPIAPITVACFDAIRA
KSWHI           -FGVRGPVQTVSTGCTSGLDAVGYAY-HAVAEGRVDVCLAGAADSPISPITMACFDAIKA
                     .*   .  ↑:.*:*:  . .      *       .

KCLFDAU         RLSGSDDPTAGYLPFDRRAAGHVPGEG-GAILAVEDAERVAERG-GKVYGSIAGT-ASFD
KCLFPEU         RLSGSDNPTAGYLPFDRRAAGHVPGEG-GAILTVEDAERAAERG-AKVYGSIAGYGASFD
KCLFACT         RISTATDPDRAYLPFDERAAGYVPGEG-GAILVLEDSAAAEARGRHDAYGELAGCASTFD
KCLFHIR         RVSRATDPGRAYLPFDVAANGYVPGEG-GAILLLEDAESAKARG-ATGYGEIAGYAATFD
KCLFGRA         LVSTVADPERAYLPFDVDASGYVPGEG-GAVLIVEDADSARARG---AERIYVRSPLRRD
KCLFNOG         GLSTSDDPRRAYLPFDAAAGGHVPGEG-GALLVLESDESARARGVTRWYGRIDGYAATFD
KCLFTCM         FLSEATDPHDAYLPFDARAAGYVPGEG-GAMLVAERADSARERDAATVYGRIAGHASTFD
KCLFCIN         -MSDSDEPNRAYLPFDRDGRGYVPGGGRGVVPPLERAEAAPARG-AEVYGE-AGPLARL-
KCLFVNZ         RLSTSEEPARGYLPFDREAQGHVPGEG-GAILVMEAAEAARERG-ARIYGEIAGYGSTFD
KCLFWHIE        ELSRATEPDRAYRPFTEAACGFAPAEG-GAVLVVEEEAAARERG-ADVRATVAGHAATFT
```

Fig 2B

```
KSGRA       TTPRNDDPAHASRPFDGTRNGFVLAEG-AAMFVLEEYEAAQRRG-AHIYAEVGGYATRSQ
KSHIR       TTPRNDDPEHASRPFDNSRNGFVLAEG-AALFVLEELEHARARG-AHVYAEISGCATRLN
KSACT       TTARNDDPEHASRPFDGTRDGFVLAEG-AAMFVLEDYDSALARG-ARIHAEISGYATRCN
KSCIN       TTPRHDAPATASRPFDSTRNGFVLGEG-AAFFVLEELHSARRRG-AHIYAEIAGYATRSN
KSVNZ       TTNRYDDPAHASRPFDGTRNGFVLGEG-AAVFVLEELESARARG-AHIYAEIAGYATRSN
KSNOG       TTPRNDTPAEASRPFDRTRNGFVLGEG-AAVFVLEEFEHARRRG-ALVYAEIAGFATRCN
KSTCM       TSANNDDPAHASRPFDRNRDGFVLGEG-SAVFVLEELSAARRRG-AHAYAEVRGFATRSN
KSDAU       TSDHNDTPETLA-PFSRSRNGFVLGEG-GAIVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSPEU       TSDHNDTPETASRPFSRSRNGFVLGEG-GAIVVLEEAEAAVRRG-ARIYAEIGGYASRGN
KSWHI       TSPNNDDPAHASRPFDADRNGFVMGEG-AAVLVLEDLEHARARG-ADVYCEVSGYATFGN
                      *     **      *.. . * ...   *    .  *.

KCLFDAU     -PPPGSGRP---SALARAVETALADAGLDRSDIAVVFADGAA-VGELDVAEAEALASVFG
KCLFPEU     -PPPGSGRP---SALARAVETALADAGLDGSDIAVVFADGAA-VPELDAAEAEALASVFG
KCLFACT     -PAPGSGRP---AGLERAIRLALNDAGTGPEDVDVVFADGAG-VPELDAAEARAIGRVFG
KCLFHIR     -PAPGSERP---PALRRAIELALADAELRPEQVDVVFADAAG-VAELDAIEAAAIRELFG
KCLFGRA     -PAPGSGRP---PALGRAAELALAEAGLTPADISVVFADGAG-VPELDRAEADTLARLFG
KCLFNOG     -PPPGSGRP---PNLLRAAQAALDDAEVGPEAVDVVFADASG-TPDEDAAEADAVRRLFG
KCLFTCM     -ARPGTGRP---TGPARAIRLALEEARVAPEDVDVVYADAAG-VPALDRAEAEALAEVFG
KCLFCIN     -PAPHSGRG---STRAHAIRTALDDAGTAPGDIRRVFADGGGRYPN-DRAEAEAISEVFG
KCLFVNZ     -PRPGSGRE---PGLRKAIELALADAGAAPGDIDVVFADAAA-VPELDRVEAEALNAVFG
KCLFWHIE    GAGRWAESR---EGLARAIQGALAEAGCRPEEVDVVFADALG-VPEADRAEALALADALG
KSGRA       -AYHMTGLKKDGREMAESIRAALDEARLDRTAVDYVNAHGSG-TKQNDRHETAAFKRSLG
KSHIR       -AYHMTGLKTDGREMAEAIRVALDLARIDPTDIDYINAHGSG-TKQNDRHETAAFKRSLG
KSACT       -AYHMTGLKADGREMAETIRVALDESRTDATDIDYINAHGSG-TRQNDRHETAAYKRALG
KSCIN       -AYHMTGLR-DGAEMAEAIRLALDEARLNPEQVDYINAHGSG-TKQNDRHETAAFKKALG
KSVNZ       -AYHMTGLRPDGAEMAEAIRVALDEARMNPTEIDYINAHGSG-TKQNDRHETAAFKKSLG
KSNOG       -AFHMTGLRPDGREMAEAIGVALAQAGKAPADVDYVNAHGSG-TRQNDRHETAAFKRSLG
KSTCM       -AFHMTGLKPDGREMAEAITAALDQARRTGDDLHYINAHGSG-TRQNDRHETAAFKRSLG
KSDAU       -AYHMTGLRADGAEMAAAITAALDEARRDPSDVDYVNAHGTA-TRQNDRHETSAFKRSLG
KSPEU       -AYHMTGLRADGAEMAAAITAALDEARRDPSDVDYVNAHGTA-TKQNDRHETSAFKRSLG
KSWHI       -AYHMTGLTKEGLEMARAIDTALDMAELDGSAIDYVNAHGSG-TQQNDRHETAAVKRSLG
             .   :          :   **  :      :  : *.. .    *  *: :    :*
```

Fig 2c

```
KCLFDAU         P--HRVPVTVPKTLTGRLYSGAGPLDVATGLLALRDEVVPATGHVH-PDPDLPLDVVTGR
KCLFPEU         P--RRVPVTVPKTLTGRLYSGAGPLDVATALLALRDEVVPATAHVD-PDPDLPLDVVTGR
KCLFACT         R--EGVPVTVPKTITGRLYSGGGPLDVVTALMSLREGVIAPTAGVTSVPREYGIDLVLGE
KCLFHIR          P--SGVPVTAPKTMTGRLYSGGGPLDLVAALLAIRDGVIPPTVHTAEPVPEHQLDLVTGD
KCLFGRA          P--RGVPVTAPKALTGRLCAGGGPADLAAALLALRDQVIPATGRHRAVPDAYALDLVTGR
KCLFNOG          P--YGVPVTAPKTMTGRLSAGGAALDVATALLALREGVVPPTVNVSRPRPEYELDLVLA-
KCLFTCM          P--GAVPVTAPKTMTGRLYAGGAALDVATALLSIRDCVVPPTVGTGAPAPGLGIDLVLHQ
KCLFCIN          P--GRVPVTCPRTMTGRLHSGAAPLDVACALLAMRAGVIPPTVHID-PCPEYDLDLVLYQ
KCLFVNZ          T--GAVPVTAPKTMTGRLYSGAAPLDLAAAFLAMDEGVIPPTVNVE-PDAAYGLDLVVGG
KCLFWHIE         PHAARVPVTAPKTGTGRAYCAAPVLDVATAVLAMEHGLIPPTPHVL--DVCHDLDLVTGR
KSGRA            EHAYAVPVSSIKSMGGHSLGAIGSIEIAASVLAIEHNVVPPTANLHTPDPECDLDYVPLT
KSHIR            EHAYRTPVSSIKSMVGHSLGAIGSIEVAACALAIEHGVVPPTANLHEPDPECDLDYVPLT
KSACT            EHARRTPVSSIKSMVGHSLGAIGSLEIAACVLALEHGVVPPTANLRTSDPECDLDYVPLE
KSCIN            EHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLT
KSVNZ            DHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEHNVVPPTGNLHTPDPECDLDYVR-S
KSNOG            DHAYRVPVSSIKSMIGHSLGAIGSLEIAASVLAITHDVVPPTANLHEPDPECDLDYVPLR
KSTCM            QRAYDVPVSSIKSMIGHSLGAIGSLELAACALAIEHGVIPPTANYEEPDPECDLDYVPNV
KSDAU            DHAYRVPISSVKSMIGHSLGAAGSLEVAATALAVEYGAIPPTANLHDPDPELDLDYVPLT
KSPEU            EHAYRVPISSIKSMIGHSLGAVGSLEVAATALAVEYGVIPPTANLHDPDPELDLDYVPLT
KSWHI            EHAYATPMSSIKSMVGHSLGAIGSIELAACVLAMAHQVVPPTANYTTPDPECDLDYVPRE
                      .*::  ::  *:   .    ::.   :::    :..*           :* *

KCLFDAU          PRAMADARAALVVARGHGGFNSALVVRGAA-------
KCLFPEU          PRSLADARAALLVARGYGGFNSALVVRGAA-------
KCLFACT          PRSTAPRTA-LVLARGRWGFNSAAVLRRFAPTP----
KCLFHIR          PRHQQLGTA-LVLARGKWGFNSAVVVRGVTG------
KCLFGRA          PREAALSAA-LVLARGRHGFNSAVVVTLRGSDHRRPT
KCLFNOG          PRRTPLARA-LVLARGRGGFNAAMVVAGPRAETR---
KCLFTCM          PRELRVDTA-LVVARGMGGFNSALVVRRHG-------
KCLFCIN          VRPAALRTA-LGGARGHGGFNSALVVRAGQ-------
KCLFVNZ          PRTAEVNTA-LVIARGHGGFNSAMVVRSAN-------
KCLFWHIE         ARPAEPRTA-LVLARGLMGSNSALVLRRGAVPPEGR-
KSGRA            AREQRVDTV-LTVGSGFGGFQSAMVLHRPEEAA----
KSHIR            AREQRVDTV-LSVGSGFGGFQSAMVLRRLGGANS---
KSACT            ARERKLRSV-LTVGSGFGGFQSAMVLRDAETAGAAA-
KSCIN            ARDQRVDSV-LTVGSGFGGFQSAMVLTSAQ---RSTV
KSVNZ            CREQLTDSV-LTVGSGFGGFQSAMVLARPE---RKIA
KSNOG            ARACPVDTV-LTVGSGFGGFQSAMVLCGPGSRGRSAA
KSTCM            AREQRVDTV-LSVGSGFGGFQSAAVLARPKEIRS---
KSDAU            AREKRVRHA-LTVGSGFGGFQSAMLLSRPER------
KSPEU            AREKRVRHA-LTVGSGFGGFQSAMLLSRLER------
KSWHI            ARERTLRHV-LSVGSGFGGFQSAVVLSGSEGGLR---
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mole:~/ks2%
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Fig 2D

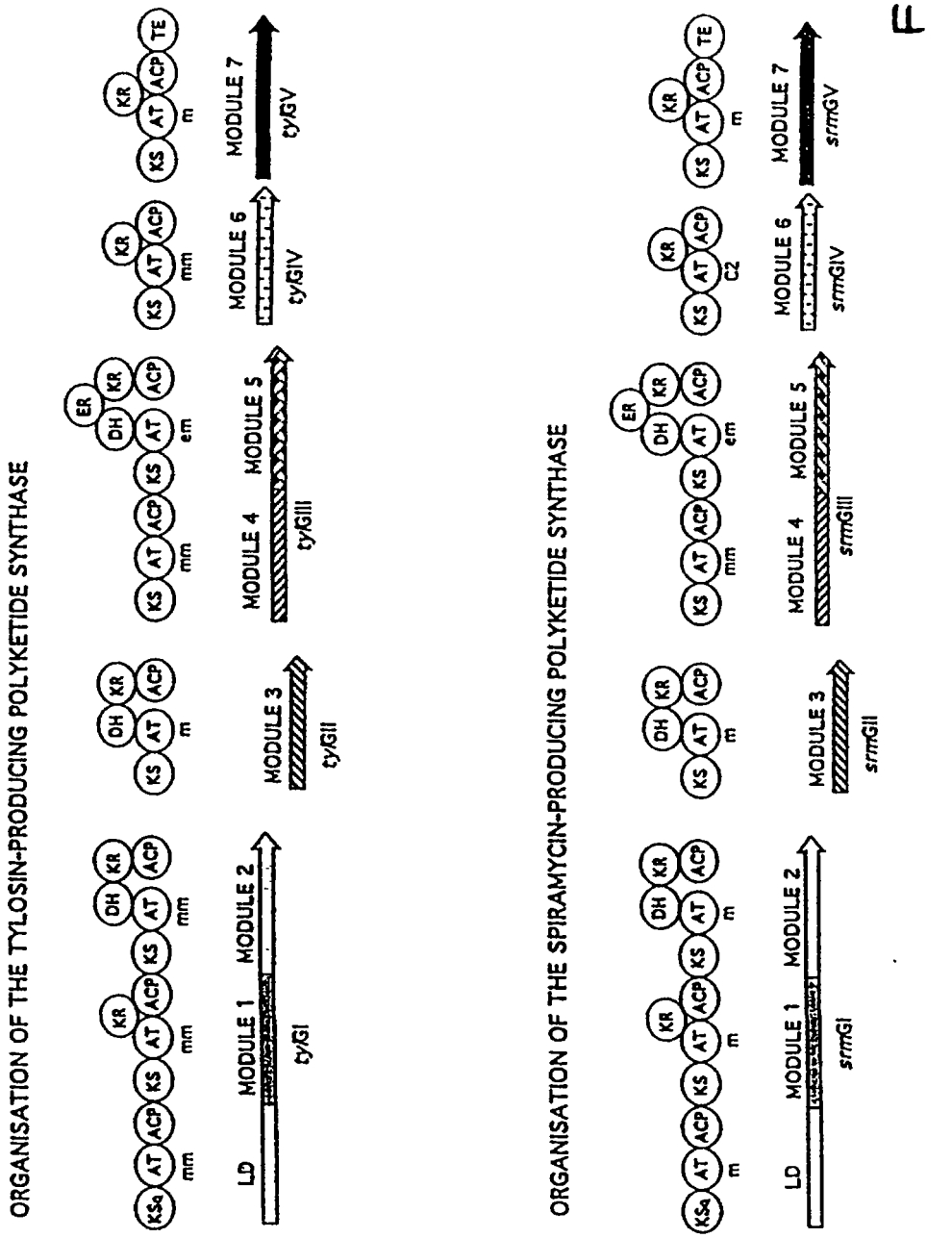

ORGANISATION OF THE TYLOSIN-PRODUCING POLYKETIDE SYNTHASE
LD
MODULE 1
MODULE 2
MODULE 3
MODULE 4
MODULE 5
MODULE 6
MODULE 7
tylGI
tylGII
tylGIII
tylGIV
tylGV
ORGANISATION OF THE SPIRAMYCIN-PRODUCING POLYKETIDE SYNTHASE
srmGI
srmGII
srmGIII
srmGIV
srmGV

Fig 3A

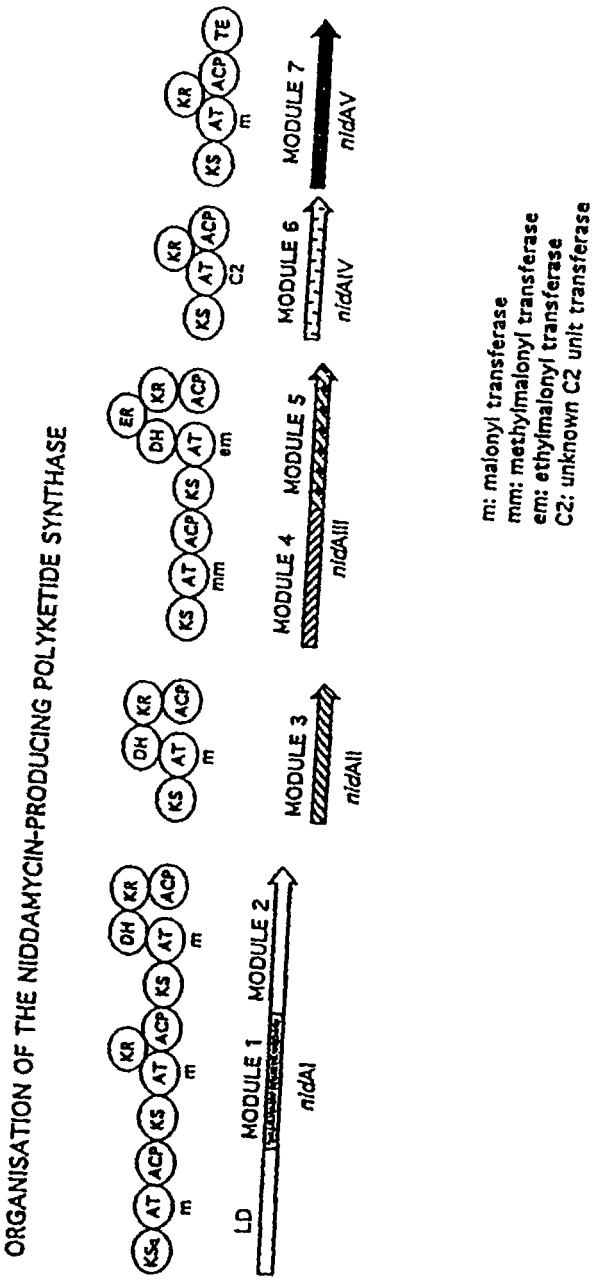

ORGANISATION OF THE NIDDAMYCIN-PRODUCING POLYKETIDE SYNTHASE
LD
MODULE 1
MODULE 2
MODULE 3
MODULE 4
MODULE 5
MODULE 6
MODULE 7
nidAI
nidAII
nidAIII
nidAIV
nidAV
m: malonyl transferase
mm: methylmalonyl transferase
em: ethylmalonyl transferase
C2: unknown C2 unit transferase

Fig 3B

```
           1                                                    50
niddamycin ~~~~~~~~~ ~~~~~~~~~~ MAGHGDATAQ KAQDAEKSED GSDAIAVIGM
platenolide ~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~MS GELAISRSDD RSDAVAVVGM
monensin   ~~~~~~~~~ ~~~~~~~~~~ ~~~~~~MAAS ASASPSGPSA GPDPIAVVGM
oleandomycin~~~~~~~~~ ~~~~~~~~~~ ~~~~~~~~~~ ~~~MHVPGEE NGHSIAIVGI
tylosin    MSSALRRAVQ SNCGYGDLMT SNTAAQNTGD QEDVDGPDST HGGEIAVVGM

           51                                                   100
niddam...  SCRFPGAPGT AEFWQLLSSG ADAVVTAADG RRR..... .....GTIDA
platenol.  ACRFPGAPGI AEFWKLLTDG RDAIGRDADG RRR..... .....GMIEA
monensin   ACRLPGAPDP DAFWRLLSEG RSAVSTAPPE RRRADSGLHG P...GGYLDR
oleandom   ACRLPGSATP QEFWRLLADS ADALDEPPAG RFPTGSLSSP PAPRGGFLDS
tylosin    SCRLPGAAGV EEFWELLRSG RGMPTRQDDG TWRAA..... .......LED

           101                                                  150
niddam...  PADFDAAFFG MSPREAAATD PQQRLVLELG WEALEDAGIV PESLRGEAAS
platenol.  PGDFDAAFFG MSPREAAETD PQQRLMLELG WEALEDAGIV PGSLRGEAVG
monensin   IDGFDADFFH ISPREAVAMD PQQRLLLELS WEALEDAGIR PPTLARSRTG
oleandom   IDTFDADFFN ISPREAGVLD PQQRLALELG WEALEDAGIV PRHLRGTRTS
tylosin    HAGFDAGFFG MNARQAAATD PQHRLMLELG WEALEDAGIV PGDLTGTDTG

           151                                                  200
niddam...  VFVGAMNDDY ATLLH.RAGA PTDTYTATGL QHSMIANRLS YFLGLRGPSL
platenol.  VFVGAMHDDY ATLLH.RAGA PVGPHTATGL QRAMLANRLS YVLGTRGPSL
monensin   VFVGAFWDDY TDVLNLRAPG AVTRHTMTGV HRSILANRIS YAYHLAGPSL
oleandom   VFMGAMWDDY AHLAHARGEA ALTRHSLTGT HRGMIANRLS YALGLQGPSL
tylosin    VFAGVASDDY A.VLTRRSAV SAGGYTATGL HRALAANRLS HFLGLRGPSL

           201                                                  250
niddam...  VVDTGQSSSL VAVALAVESL RGGTSGIALA GGVNLVLAEE GS.AAMERVG
platenol.  AVDTAQSSSL VAVALAVESL RAGTSRVAVA GGVNLVLADE GT.AAMERLG
monensin   TVDTAQSSSL VAVHLACESI RSGDSDIAFA GGVNLICSPR TTELAAARFG
oleandom   TVDTGQSSSL AAVHMACESL ARGESDLALV GGVNLVLDPA GT.TGVERFG
tylosin    VVDSAQSASL VAVQLACESL RRGETSLAVA GGVNLILTEE ST.TVMERMG

           251                                                  300
niddam...  ALSPDGRCHT FDARANGYVR GEGGAIVVLK PLADALADGD RVYCVVRGVA
platenol.  ALSPDGRCHT FDARANGYVR GEGGAAVVLK PLADALADGD PVYCVVRGVA
monensin   GLSAAGRCHT FDARADGFVR GEGGGLVVLK PLAAARRDGD TVYCVIRGSA
oleandom   ALSPDGRCYT FDSRANGYAR GEGGVVVVLK PTHRALADGD TVYCEILGSA
tylosin    ALSPDGRCHT FDARANGYVR GEGGGAVVLK PLDAALADGD RVYCVIKGGA

           301                                                  350
niddam...  TGNDGGGPGL TVPDRAGQEA VLRAACDQAG VRPADVRFVE LHGTGTPAGD
platenol.  VGNDGGGPGL TAPDREGQEA VLRAACAQAR VDPAEVRFVE LHGTGTPVGD
monensin   VNSDGTTDGI TLPSGQAQQD VVRLACRRAR ITPDQVQYVE LHGTGTPVGD
oleandom   LNNDGATEGL TVPSARAQAD VLRQAWERAR VAPTDVQYVE LHGTGTPAGD
tylosin    VNNDGGGASL TTPDREAQEA VLRQAYRRAG VSTGAVRYVE LHGTGTRAGD
```

Fig 4A

```
            351                                                 400
niddam...   PVEAEALGAV YGTGRP..AN EPLLVGSVKT NIGHLEGAAG IAGFVKAALC
platenol.   PVEAHALGAV HGSGRP..AD DPLLVGSVKT NIGHLEGAAG IAGLVKAALC
monensin    PIEAAALGAA LGQDAA..RA VPLAVGSAKT NVGHLEAAAG IVGLLKTALS
oleandom    PVEAEGLGTA LGTARP..AE APLLVGSVKT NIGHLEGAAG IAGLLKTVLS
tylosin     PVEAAALGAV LGAGADSGRS TPLAVGSVKT NVGHLEGAAG IVGLIKATLC

            401                                                 450
niddam...   LHERALPASL NFETPNPAIP LERLRLKVQT AHAALQPGTG GGPLLAGVSA
platenol.   LRERTLPGSL NFATPSPAIP LDQLRLKVQT AAAELPLAPG GAPLLAGVSS
monensin    IHHRRLAPSL NFTTPNPAIP LADLGLTVQQ DLADWP..RP EQPLIAGVSS
oleandom    IKNRHLPASL NFTSPNPRID LDALRLRVHT AYGPWP..SP DRPLVAGVSS
tylosin     VRKGELVPSL NFSTPNPDIP LDDLRLRVQT ERQEW.NEED DRPRVAGVSS

            451                                                 500
niddam...   FGMGGTNCHV VLEETPGG.. .......... .......... ...RQPAE.T
platenol.   FGIGGTNCHV VLEHLPSR.. .......... .......... ...PTPAV.S
monensin    FGMGGTNGHV VVA....AAP DSVAVPEPVG VPERVEVPEP VVVSEPVVVP
oleandom    FGMGGTNCHV VLSELRNAGG DGAGKGPYTG TEDRLGATEA EKRPDPATGN
tylosin     FGMGGTNVHL VIAEAPAAAG SSGAGGSGAG SGAGISAVSG VV........

            501                                                 550
niddam...   GQADACLFSA SPMLLLSARS EQALRAQAAR LREHL..EDS GADPLDIAYS
platenol.   VAAS...LPD VPPLLLSARS EGALRAQAVR LGETV..ERV GADPRDVAYS
monensin    TPWP...... .....VSAHS ASALRAQAGR LRTHLAAHRP TPDAARVGHA
oleandom    GPDPAQDTHR YPALILSARS DAALRAQAER LRHHL.EHSP GQRLRDTAYS
tylosin     .......... ..PVVVSGRS RVVVREAAGR LAE..VVEAG GVGLADVAVT

            551                                                 600
niddam...   LATTRTRFEH RAAVPCGDPD RLSSALAALA AGQTPRGVRI GS..TDADGR
platenol.   LASTRTLFEH RAVVPCGGRG ELVAALGGFA AGRVSGGVRS GR..A.VPGG
monensin    LATTRAPLAH RAVLLGGDTA ELLGSLDALA EGAETASIVR GEAYT..EGR
oleandom    LATRRQVFER HAVVTGHDRE DLLNGLRDLE NGLPAPQVLL GRTPTPEPGG
tylosin     MAD.RSRFGY RAVVLARGEA ELAGRLRALA GGDPDAGVVT G...AVLDGG

            601                                                 650
niddam...   LALLFTGQGA QHPGMGQELY TTDPHFAAAL DEVCEELQRC GTQNLREVMF
platenol.   VGVLFTGQGA QWVGMGRGLY AGGGVFAEVL DEVLSMVGEV DGRSLRDVMF
monensin    TAFLFSGQGA QRLGMGRELY AVFPVFADAL DEAFAALDVH LDRPLREIVL
oleandom    LAFLFSGQGS QQPGMGKRLH QVFPGFRDAL DEVCAELDTH LGRLL.....
tylosin     VVVGAAPGGA GAAGGAGAAG GAGGGGVVLV FPGQGTQWVG MGAGLLGSSE

            651                                                 700
niddam...   TPDQPD.... .......... .......... LLDRTEYTQP ALFALQTALY
platenol.   GDVDVDAGAG ADAGAGAGAG VGSGSGSVGG LLGRTEFAQP ALFALEVALF
monensin    GETDSGGNVS GENVIGEGA. ......DHQA LLDQTAYTQP ALFAIETSLY
oleandom    .GPEAGPPLR DVMFAERGT. ......AHSA LLSETHYTQA ALFALETALF
tylosin     VFAASMRECA RALSVHVGWD LLEVVSGGAG .LERVDVVQP VTWAVMVSLA

            701                                                 ↓ 750
niddam...   RTLTARGTQA HLVLGHSVGE ITAAHIAGVL DLPDAARLIT ARAHVMGQLP
platenol.   RALEARGVEV SVVLGHSVGE VAAATVAGVL SLGDAVRLVV ARGGLMGGLP
monensin    RLAASFGLKP DYVLGHSVGE IAAAHVAGVL SLPDASALVA TRGRLMQAVR
oleandom    RLLVQWGLKP DHLAGHSVGE IAAAHAAGIL DLSDAAELVA TRGALMRSLP
tylosin     RYWQAMGVDV AAVVGHSQGE IAAATVAGAL SLEDAAAVVA LRAGLIGRYL
```

↑ Fig 4B

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          751                                                  800
niddam... HG.GAMLSVQ AAEHDLLDQLA HTHG..VEIA AVNGPTHCVL SGPRTALEET
platenol. VG.GGMWSVG ASESVVRGVV EGLGEWVSVA AVNGPRSVVL SGDVGVLESV
monensin  AP.GAMAAWQ ATADEAAEQL AGHERHVTVA AVNGPDSVVV SGDRATVDEL
oleandom  GG.GVMLSVQ APESEVAPLL LGREAHVGLA AVNGPDAVVV SGERGHVAAI
tylosin   AGRGAMAAVP LPAGEVEAGL .AKWPGVEVA AVNGPASTVV SGDRRAVAGY

          801                                                  850
niddam... AQHLREQNVR HTWLKVSHAF HSALMDPMLG AFRDTLNTLN Y..QPPTIPL
platenol. VASLMGDGVE YRRLDVSHGF HSVLMEPVLG EFRGVVESLE FGRVRPGVVV
monensin  TAAWRGRGRK AHHLKVSHAF HSPHMDPILD ELRAVAAGLT FHE..PVIPV
oleandom  EQILRDRGRK SRYLRVSHAF HSPLMEPVLE EFAEAVAGLT FRA..PTTPL
tylosin   VAVCQAEGVQ ARLIPVDYAS HSRHVEDLKG ELERVLSGI. .RPRSPRVPV

          851                                                  900
niddam... ISNLTGQIA. .....DPNHL CTPDYWIDHA RHTVRFADAV QTAHHQGTTT
platenol. VSGVSGGVV. .....GSGEL GDPGYWVRHA REAVRFADGV GVVRGLGVGT
monensin  VSNVTGELVT ATATGSGAGQ ADPEYWARHA REPVRFLSGV RGLCERGVTT
oleandom  VSNLTG.... ..APVDDRTM ATPAYWVRHV REAVRFGDGI RALGKLGTGS
tylosin   CSTVAGEQPG EPVF...... .DAGYWFRNL RNRVEFSAVV GGLLEEGHRR

          901                                                  950
niddam... YLEIGPHPTL TTLLHHTL.. .DNP..... .........T TIPTLHRERP
platenol. LVEVGPHGVL TGMAGECLGA GDDV..... .........V VVPAMRRGRA
monensin  FVELGPDAPL SAMARDCFPA P......... .ADRSRPRPA AIATCRRGRD
oleandom  FLEVGPDGVL TAMARACVTA APEPGHRGEQ GADADAHTAL LLPALRRGRD
tylosin   FIEVSAHPVL V......... .....HAIEQ TAEAADRSVH ATGTLRRQDD

          951
niddam... EPETLTQAIA AVGVRTDGID WAVLCGASRP RRVELPTYAF
platenol. EREVFEAALA TVFTRDAGLD ATALHTGSTG RRIDLPTTPF
monensin  EVATFLRSLA QAYVRGADVD FTRAYGATAT RRFPLPTYPF
oleandom  EARSLTEAVA RLHLHGVPMD WTSVLGGDVS .RVPLPTYAF
tylosin   SPHRLLTSTA EAWAHGATLT WDPAL..PPG HLTTLPTYPF
```

niddam: niddamycin; platenol: platenolide I (spiramycin); oleandom: oleandomycin.

Fig 4c

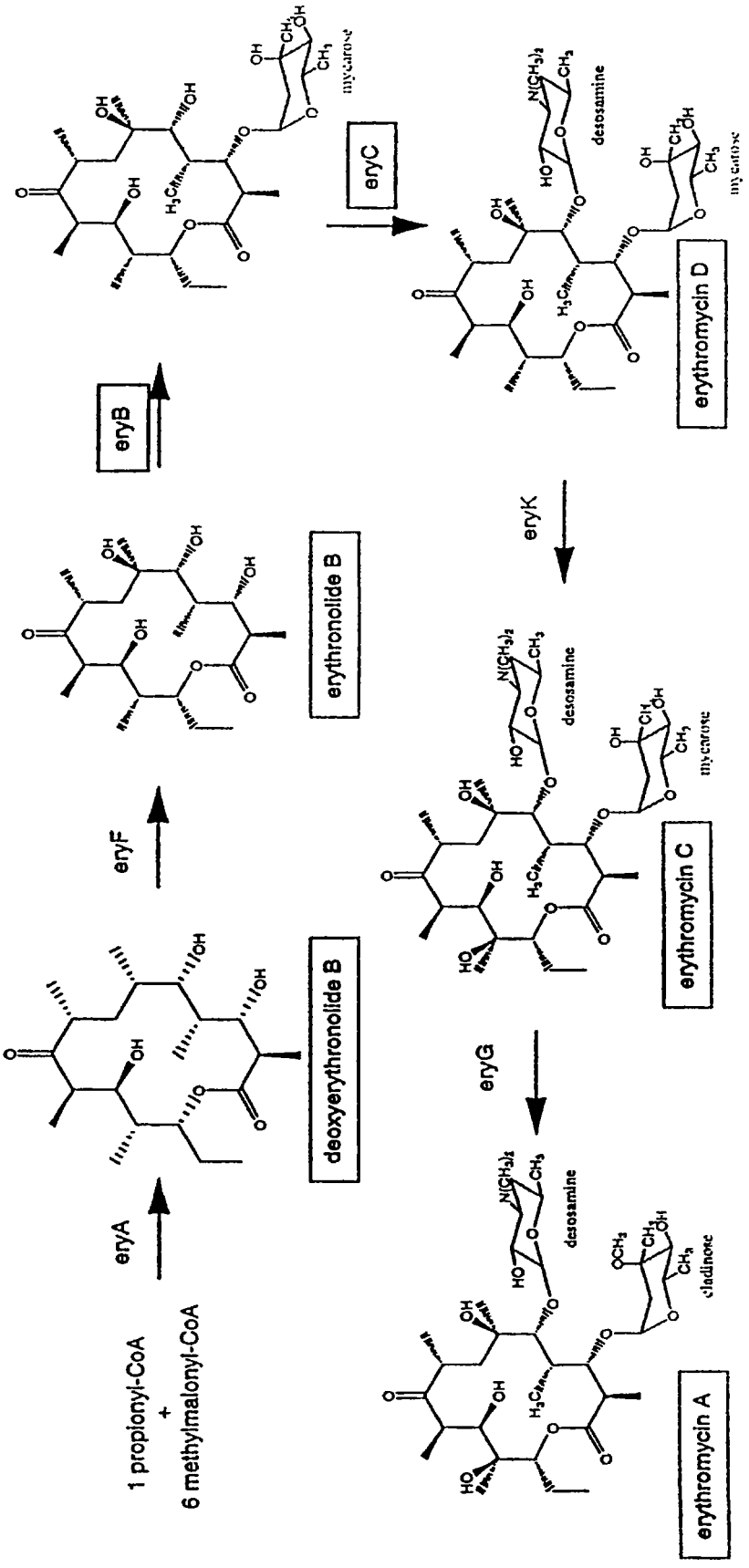

1 propionyl-CoA
+
6 methylmalonyl-CoA
eryA
deoxyerythronolide B
eryF
erythronolide B
eryB
eryC
erythromycin D
eryK
erythromycin C
eryG
erythromycin A
desosamine
mycarose
cladinose

Fig. 5

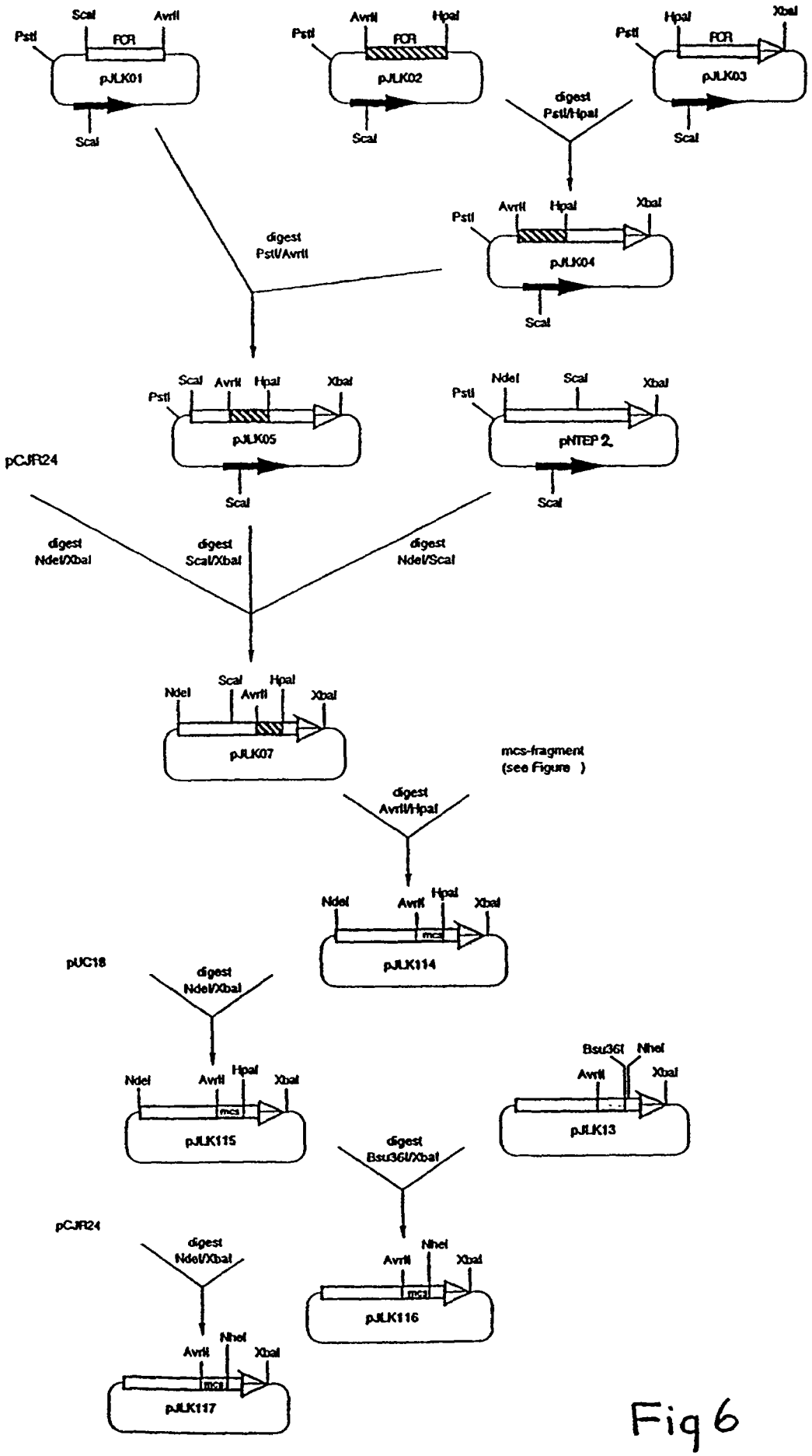

ScaI
AvrII
PstI
PCR
pJLK01
ScaI
AvrII
HpaI
PstI
PCR
pJLK02
ScaI
HpaI
XbaI
PstI
PCR
pJLK03
ScaI
digest
PstI/HpaI
AvrII
HpaI
XbaI
PstI
pJLK04
ScaI
digest
PstI/AvrII
ScaI
AvrII
HpaI
XbaI
PstI
pJLK05
ScaI
NdeI
ScaI
XbaI
PstI
pNTEP 2
ScaI
pCJR24
digest
NdeI/XbaI
digest
ScaI/XbaI
digest
NdeI/ScaI
NdeI
ScaI
AvrII
HpaI
XbaI
pJLK07
mcs-fragment
(see Figure)
digest
AvrII/HpaI
NdeI
AvrII
HpaI
XbaI
mcs
pJLK114
pUC18
digest
NdeI/XbaI
NdeI
AvrII
HpaI
XbaI
mcs
pJLK115
Bsu36I
NheI
AvrII
XbaI
pJLK13
digest
Bsu36I/XbaI
pCJR24
digest
NdeI/XbaI
AvrII
NheI
XbaI
mcs
pJLK116
AvrII
NheI
XbaI
mcs
pJLK117

Fig 6

Figure 7

forward (P1f):

5'-CTA GGC CGG GCC GGA CTG GTA GAT CTG CCT ACG TAT CCT TTC CAG GGC AAG CGG TTC TGG CTG CAG CCG GAC CGC ACT AGT CCT CGT GAC GAG

GGA GAT GCA TCG AGC CTG AGG GAC CGG TT-3'

backward (P1b):

5'-AAC CGG TCC CTC AGG CTC GAT GCA TCT CCC TCG TCA CGA GGA CTA GTG CGG TCC GGC TGC AGC CAG AAC CGC TTG CCC TGG AAA GGA TAC GTA

GGC AGA TCT ACC AGT CCG GCC CGG C-3'

oligos annealed:

CTAGGCCGGGCCGGACTGGTAGATCTGCCTACGTATCCTTTCCAGGGCAAGCGGTTCTGGCTGCAGCCGGACCGCACTAGTCCTCGTGACGAGGGAGATGCATCGAGCCTGAGGGACCGGTT
CGGCCCGGCCTGACCATCTAGACGGATGCATAGGAAAGGTCCCGTTCGCCAAGACCGACGTCGGCCTGGCGTGATCAGGAGCACTGCTCCCTCTACGTAGCTCGGACTCCCTGGCCAA

AvrII	BglII	SnaBI	PstI	SpeI	NsiI	Bsu36I	HpaI