The alignment was done on 3 Protein sequences.
Character to show that a position in the alignment is perfectly conserved: '*'
Character to show that a position is well conserved: '.'

Alignment

```
ADIPROT     MSVFDSKFKGIHVYSEIGELESVLVHEPGREIDYITPARLDELLFSAILE    50
ARTADIPRO   MSVFDSKFKGIHVYSEIGELESVLVHEPGREIDYITPARLDELLFSAILE    50
HOMADIPRO   MSVFDSKFNGIHVYSEIGELETVLVHEPGREIDYITPARLDELLFSAILE    50
            ********.***********.****************************

ADIPROT     SHDARKEHKQFVAELKANDINVVELIDLVAETYDLASQEAKDKLIEEFLE   100
ARTADIPRO   SHDARKEQSQFVAILKANDINVVETIDLVAETYDLASQEAKDRLIEEFLE   100
HOMADIPRO   SHDARKEHQSFVKIMKDRGINVVELTDLVAETYDLASKAAKEEFIETFLE   100
            *******. **  .*...***** .**********..**. .**.***

ADIPROT     DSEPVLSEEHKVVVRNFLKAKKTSRKLVEIMMAGITKYDLGIEADHELIV   150
ARTADIPRO   DSEPVLSEAHKKVVRNFLKAKKTSRKLVELMMAGITKYDLGVEADHELIV   150
HOMADIPRO   ETVPVLTEANKKAVRAFLLSKPT-HEMVEFMMSGITKYELGVESENELIV   149
            .. ***.*..* .**.** .* * ...**.**.*****.**.*...****

ADIPROT     DPMPNLYFTRDPFASVGNGVTIHYMRYKVRQRETLFSRFVFSNHPKLINT   200
ARTADIPRO   DPMPNLYFTRDPFASVGNGVTIHFMRYKVRRRETLFSRFVFRNHPKLVNT   200
HOMADIPRO   DPMPNLYFTRDPFASVGNGVTIHFMRYIVRRRETLFARFVFRNHPKLVKT   199
            **********************.*** **.*****.****.*****..*

ADIPROT     PWYYDPSLKLSIEGGDVFIYNNDTLVVGVSERTDLQTVTLLAKNIVANKE   250
ARTADIPRO   PWYYDPAMKLSIEGGDVFIYNNDTLVVGVSERTDLDTVTLLAKNLVANKE   250
HOMADIPRO   PWYYDPAMKMPIEGGDVFIYNNETLVVGVSERTDLDTITLLAKNIKANKE   249
            ******..*..**********.**********.*.******. ****

ADIPROT     CEFKRIVAINVPKWTNLMHLDTWLTMLDKDKFLYSPIANDVFKFWDYDLV   300
ARTADIPRO   CEFKRIVAINVPKWTNLMHLDTWLTMLDKNKFLYSPIANDVFKFWDYDLV   300
HOMADIPRO   VEFKRIVAINVPKWTNLMHLDTWLTMLDKNKFLYSPIANDVFKFWDYDLV   299
             ****************************.********************

ADIPROT     NGGAEPQPVENGLPLEGLLQSIINKKPVLIPIAGEGASQMEIERETHFDG   350
ARTADIPRO   NGGAEPQPVENGLPLEKLLQSIINKKPVLIPIAGEGASQMEIERETHFDG   350
HOMADIPRO   NGGAEPQPQLNGLPLDKLLASIINKEPVLIPIGGAGATEMEIARETNFDG   349
            ********  *****. **.*****.******.*.**..***.***.***

ADIPROT     TNYLAIRPGVVIGYSRNEKTNAALEAAGIKVLPFHGNQLSLGMGNARCMS   400
ARTADIPRO   TNYIAIRPGVVIGYSRNEKTNAALKAAGIKVLPFHGNQLSLGMGNARCMS   400
HOMADIPRO   TNYLAIKPGLVIGYDRNEKTNAALKAAGITVLPFHGNQLSLGMGNARCMS   399
            ***.**.**.****.*********.****.********************

ADIPROT     MPLSRKDVKW  410
ARTADIPRO   MPLSRKDVKW  410
HOMADIPRO   MPLSRKDVKW  409
            **********
```

FIG. 1

ADIPROT	= *Mycoplasma arginini*
ARTADIPRO	= *Mycoplasma arthritides*
HOMADIPRO	= *Mycoplasma hominus*

FIG. 2A

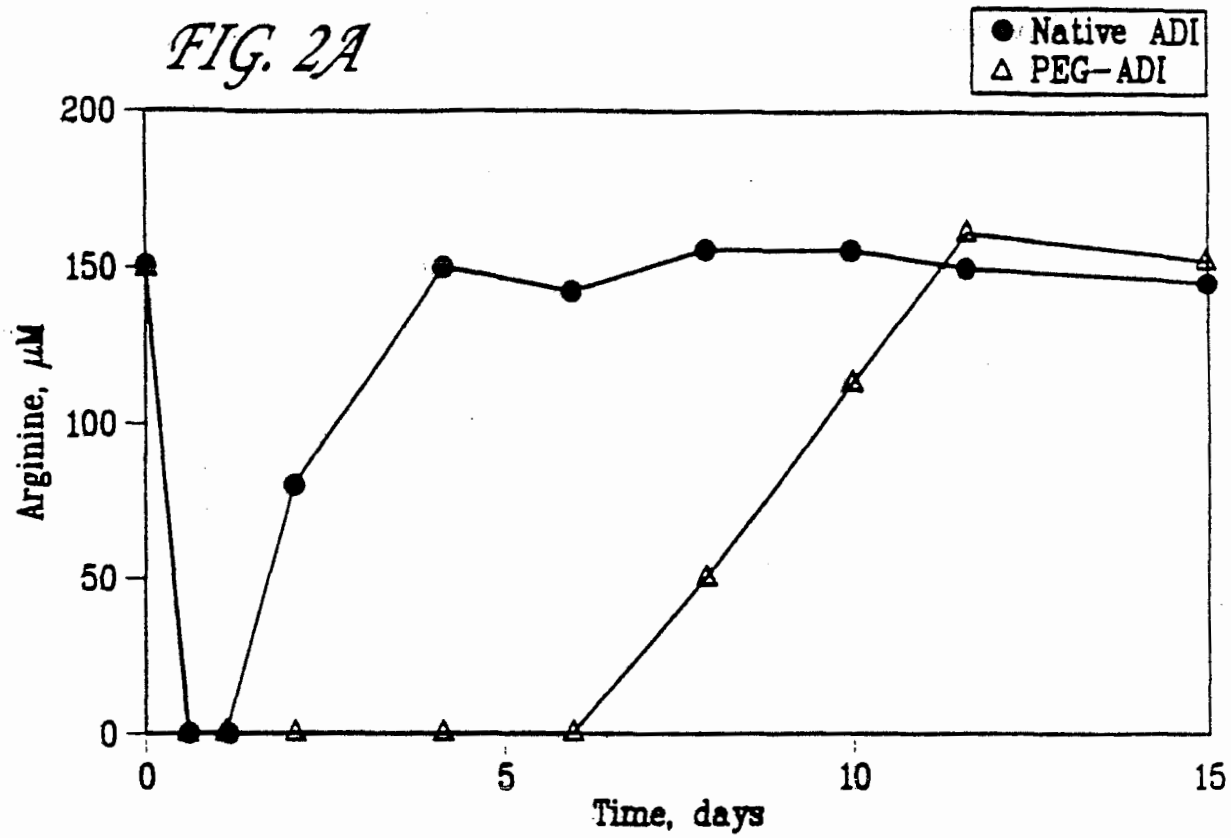

Native ADI
PEG-ADI
Arginine, μM
200
150
100
50
0
0
5
10
15
Time, days

FIG. 2B

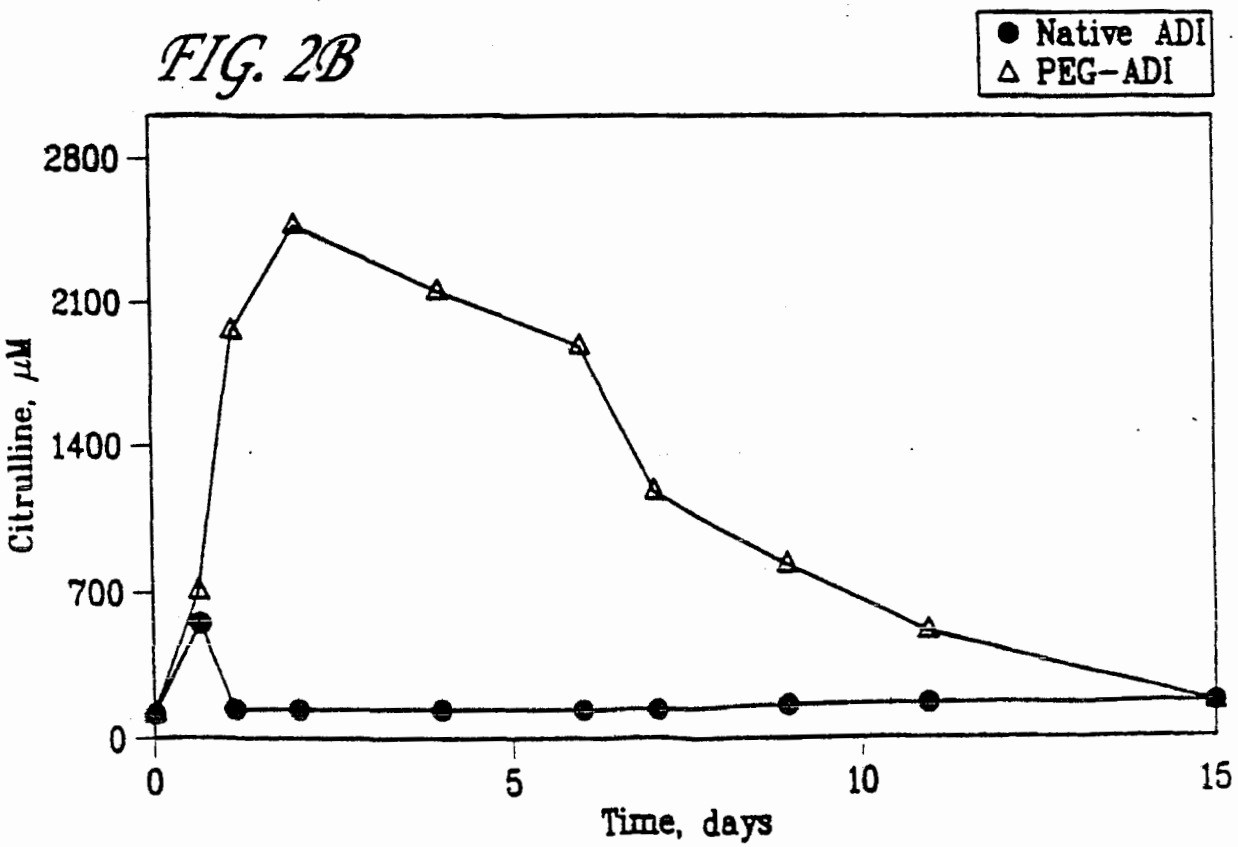

Native ADI
PEG-ADI
Citrulline, μM
2800
2100
1400
700
0
0
5
10
15
Time, days

FIG. 3

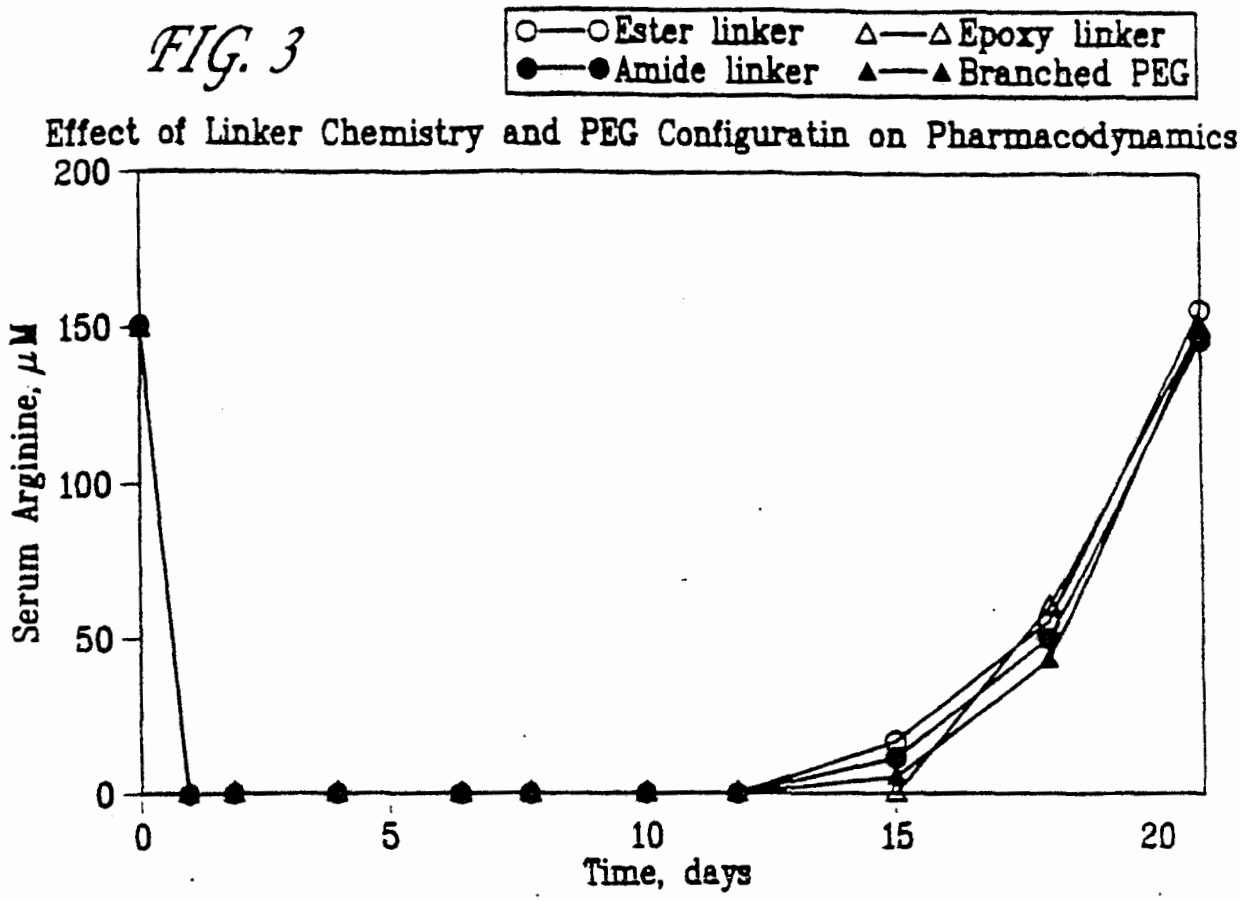
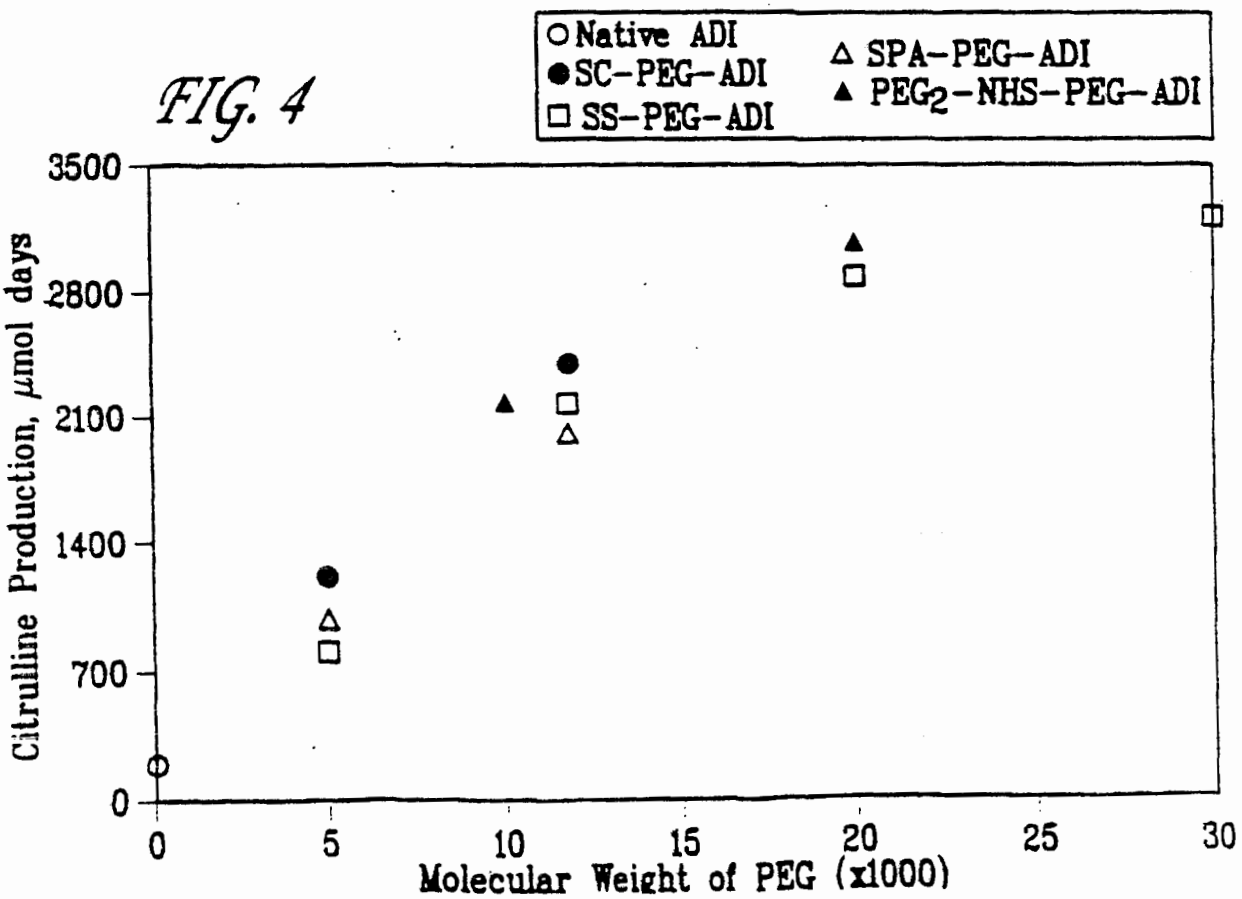

Ester linker
Epoxy linker
Amide linker
Branched PEG
Effect of Linker Chemistry and PEG Configuratin on Pharmacodynamics
Serum Arginine, μM
200
150
100
50
0
0
5
10
15
20
Time, days

FIG. 4


Native ADI
SC-PEG-ADI
SS-PEG-ADI
SPA-PEG-ADI
PEG2-NHS-PEG-ADI
Citrulline Production, μmol days
3500
2800
2100
1400
700
0
0
5
10
15
20
25
30
Molecular Weight of PEG (x1000)

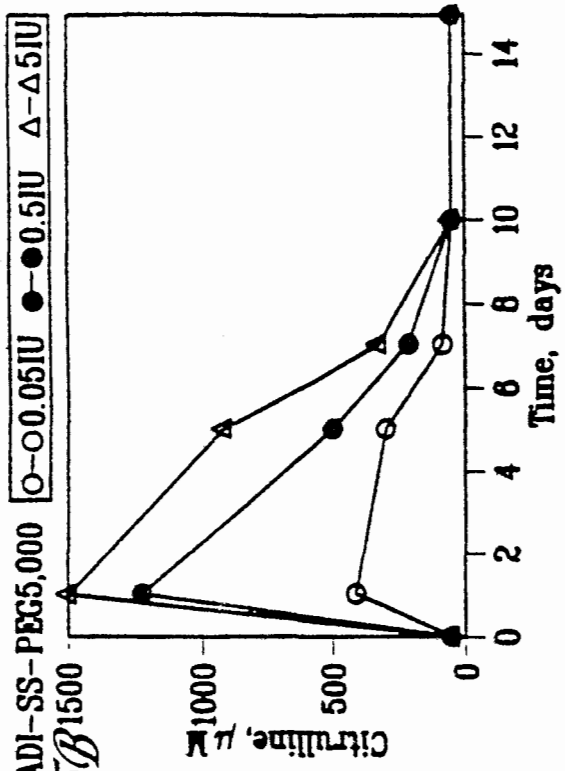


FIG. 5B

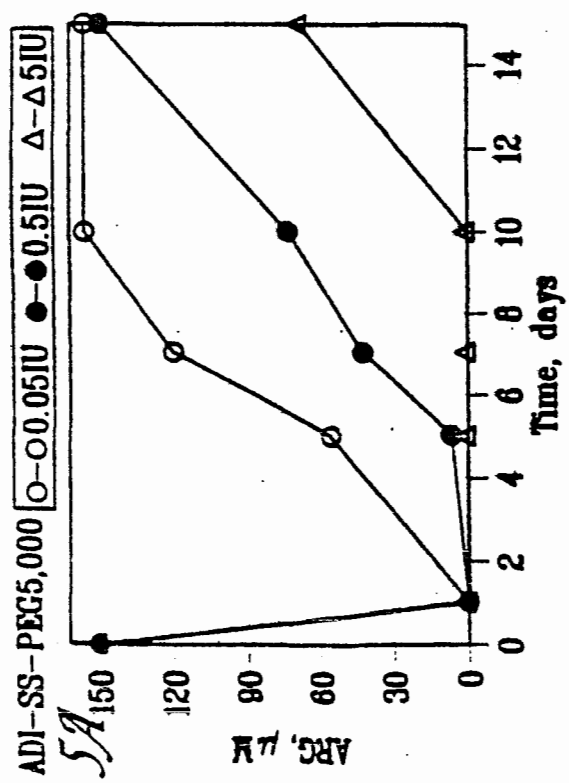


FIG. 5A

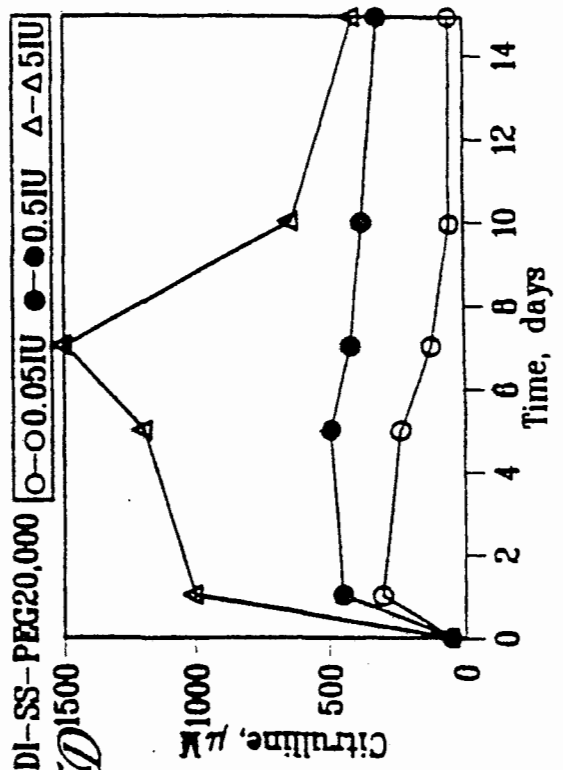


FIG. 5D

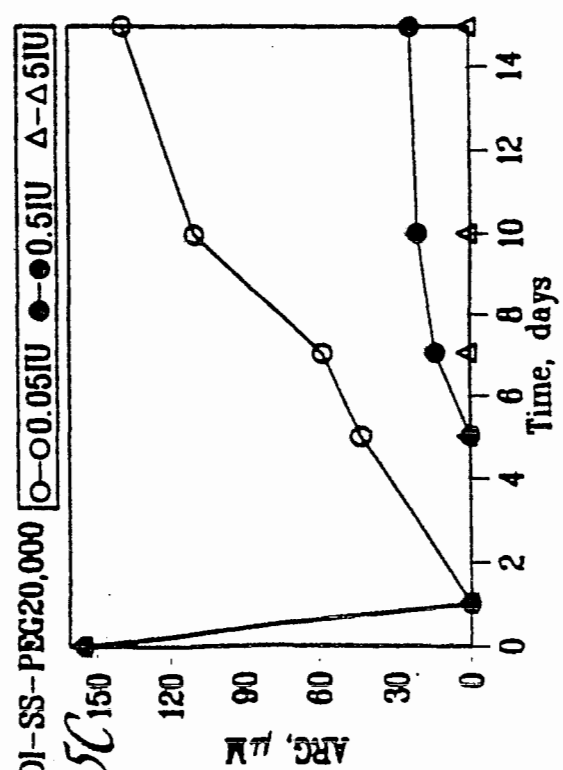


FIG. 5C

FIG. 6

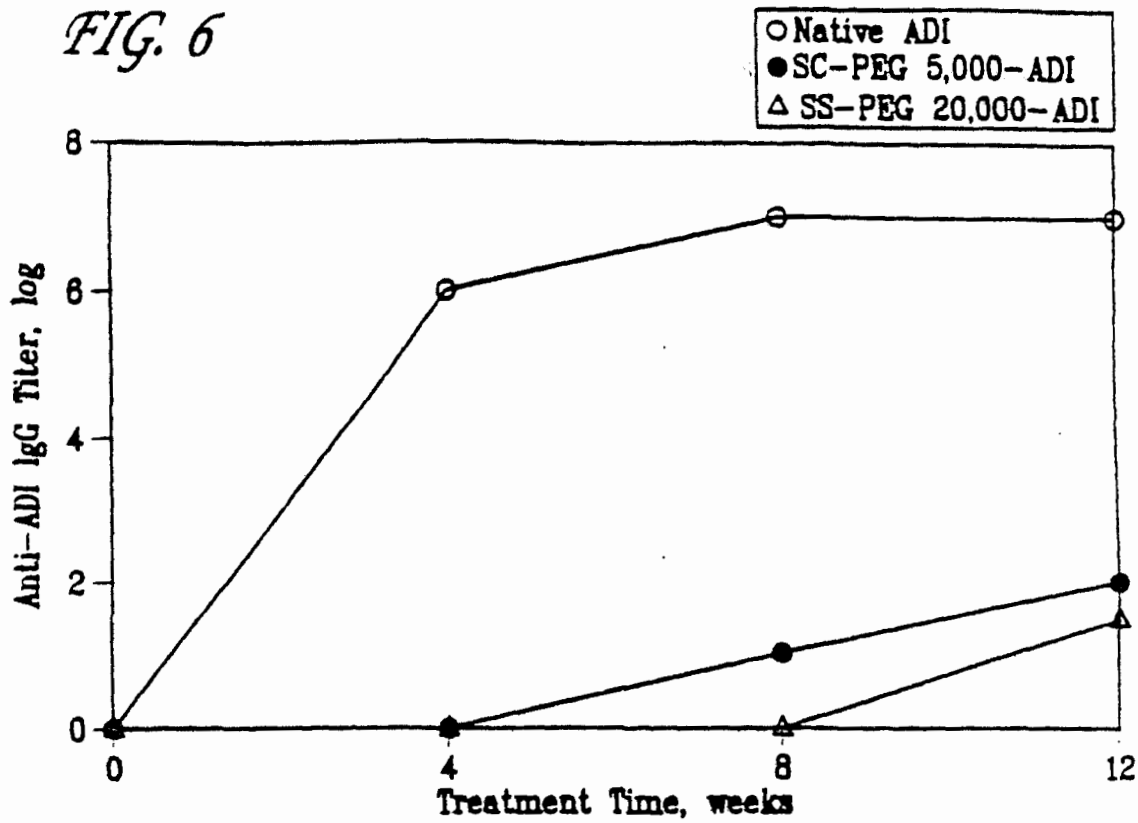

Native ADI
SC-PEG 5,000-ADI
SS-PEG 20,000-ADI
Anti-ADI IgG Titer, log
0
2
4
6
8
0
4
8
12
Treatment Time, weeks

FIG. 7

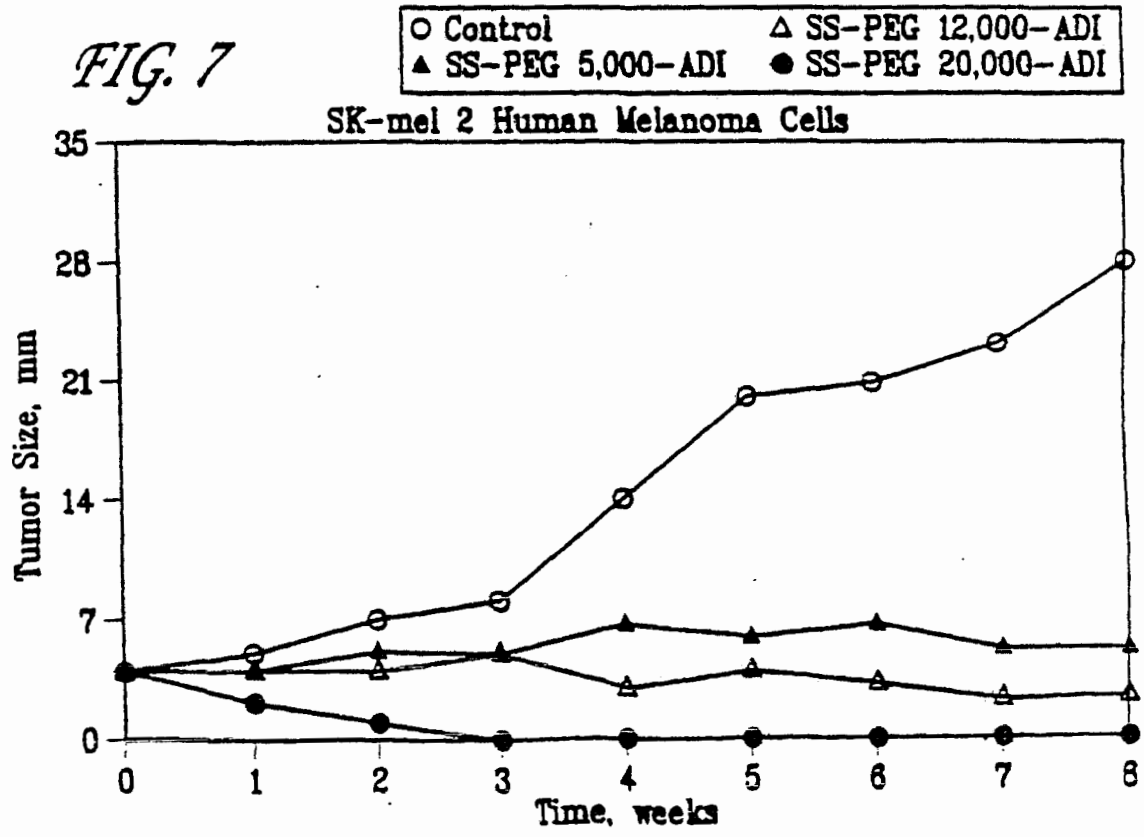

Control
SS-PEG 12,000-ADI
SS-PEG 5,000-ADI
SS-PEG 20,000-ADI
SK-mel 2 Human Melanoma Cells
Tumor Size, mm
0
7
14
21
28
35
0
1
2
3
4
5
6
7
8
Time, weeks

FIG. 8

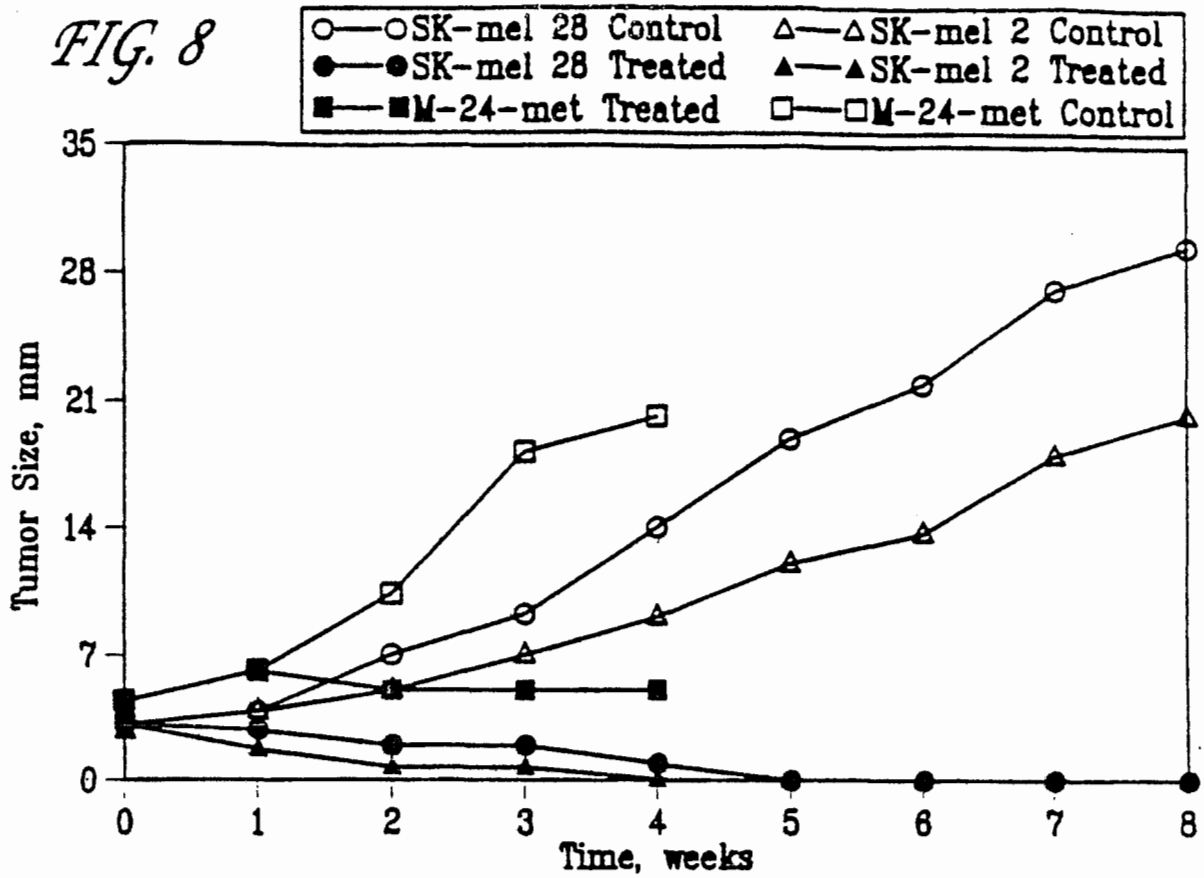
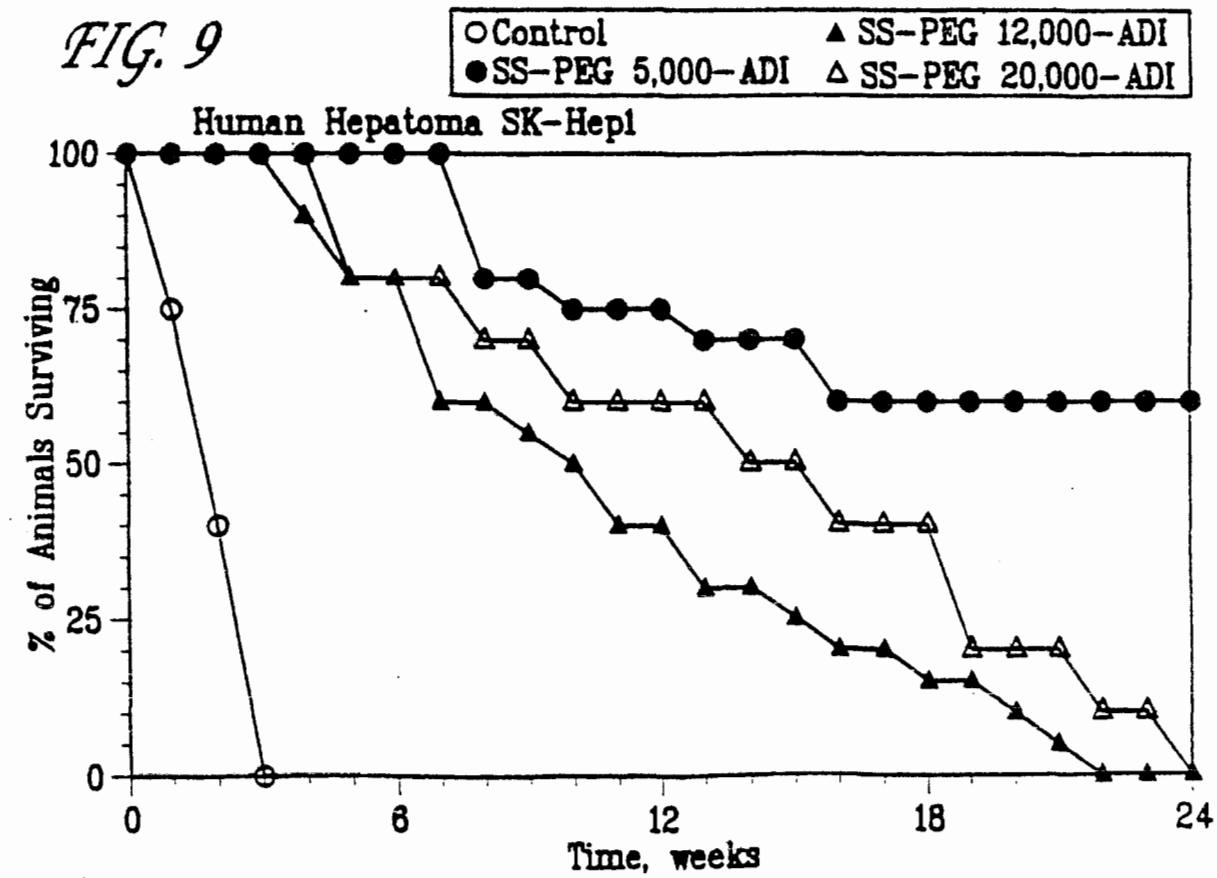

SK-mel 28 Control
SK-mel 28 Treated
M-24-met Treated
SK-mel 2 Control
SK-mel 2 Treated
M-24-met Control
Tumor Size, mm
35
28
21
14
7
0
0
1
2
3
4
5
6
7
8
Time, weeks

FIG. 9


Control
SS-PEG 5,000-ADI
SS-PEG 12,000-ADI
SS-PEG 20,000-ADI
Human Hepatoma SK-Hep1
% of Animals Surviving
100
75
50
25
0
0
6
12
18
24
Time, weeks

The alignment was done on 2 amino acid sequences.

Alignment

```
STRADIPYR  MTAQTPIHVYSEIGKLKKVLLHRPGKEIENLMPDYLERLLFDDIPFLEDA   50
STRADIPNE  MSSHPIQVFSEIGKLKKVMLHRPGKELENLLPDYLERLLFDDIPFLEDAQ  50

STRADIPYR  QKEHDAFAQALRDEGIEVLYLETLAAESLVTPEIREAFIDEYLSEANIRG  100
STRADIPNE  KEHDAFAQALRDEGIEVLYLEQLAAESLTSPEIRDQFIEEYLDEANIRDR  100

STRADIPYR  RATKKAIRELLMAIEDNQELIEKTMAGVQKSELPEIPASEKGLTDLVESN  150
STRADIPNE  QTKVAIRELLHGIKDNQELVEKTMAGIQKVELPEIPDEAKDLTDLVESEY  150

STRADIPYR  YPFAIDPMPNLYFTRDPFATIGTGVSLNHMFSETRNRETLYGKYIFTHHP  200
STRADIPNE  PFAIDPMPNLYFTRDPFATIGNAVSLNHMFADTRNRETLYGKYIFKYHPI  200

STRADIPYR  IYGGGKVPMVYDRNETTRIEGGDELVLSKDVLAVGISQRTDAASIEKLLV  250
STRADIPNE  YGGKVDLVYNREEDTRIEGGDELVLSKDVLAVGISQRTDAASIEKLLVNI  250

STRADIPYR  NIFKQNLGFKKVLAFEFANNRKFMHLDTVFTMVDYDKFTIHPEIEGDLRV  300
STRADIPNE  FKKNVGFKKVLAFEFANNRKFMHLDTVFTMVDYDKFTIHPEIEGDLHVYS  300

STRADIPYR  YSVTYDNEELHIVEEKGDLAELLAANLGVEKVDLIRCGGDNLVAAGREQW  350
STRADIPNE  VTYENEKLKIVEEKGDLAELLAQNLGVEKVHLIRCGGGNIVAAAREQWND  350

STRADIPYR  NDGSNTLTIAPGVVVVYNRNTITNAILESKGLKLIKIHGSELVRGRGGPR  400
STRADIPNE  GSNTLTIAPGVVVVYDRNTVTNKILEEYGLRLIKIRGSELVRGRGGPRCM  400

STRADIPYR  CMSMPFEREDI                                        411
STRADIPNE  SMPFEREEV                                          409
```

STRADIPYR = *Steptococcus pyogenes*

STRADIPNE = *Steptococcus pneumoniae*

FIG. 10

The alignment was done on 2 amino acid sequences.

Alignment

```
BORADIBUR  MEEEYLNPINIFSEIGRLKKVLLHRPGEELENLTPLIMKNFLFDDIPYLK   50
BORADIAFZ  MEEYLNPINIFSEIGRLKKVLLHRPGEELENLTPFIMKNFLFDDIPYLEV  50

BORADIBUR  VARQEHEVFVNILKDNSVEIEYVEDLVSEVLASSVALKNKFISQFILEAE  100
BORADIAFZ  ARQEHEVFASILKNNLVEIEYIEDLISEVLVSSVALENKFISQFILEAEI  100

BORADIBUR  IKTDGVINILKDYFSNLTVDNMVSKMISGVAREELKDCEFSLDDWVNGSS  150
BORADIAFZ  KTDFTINLLKDYFSSLTIDNMISKMISGVVTEELKNYTSSLDDLVNGANL  150

BORADIBUR  FVIDPMPNVLFTRDPFASIGNGITINKMYTKVRRRETIFAEYIFKYHSAY  200
BORADIAFZ  FIIDPMPNVLFTRDPFASIGNGVTINKMFTKVRQRETIFAEYIFKYHPVY  200

BORADIBUR  KENVPIWFNRWEETSLEGGDEFVLNKDLLVIGISERTEAGSVEKLAASLF  250
BORADIAFZ  KENVPIWLNRWEEASLEGGDELVLNKGLLVIGISERTEAKSVEKLAISLF  250

BORADIBUR  KNKAPFSTILAFKIPKNRAYMHLDTVFTQIDYSVFTSFTSDDMYFSIYVL  300
BORADIAFZ  KNKTSFDTILAFQIPKNRSYMHLDTVFTQIDYSVFTSFTSDDMYFSIYVL  300

BORADIBUR  TYNSNSNKINIKKEKAKLKDVLSFYLGRKIDIIKCAGGDLIHGAREQWND  350
BORADIAFZ  TYNPSSSKIHIKKEKARIKDVLSFYLGRKIDIIKCAGGDLIHGAREQWND  350

BORADIBUR  GANVLAIAPGEVIAYSRNHVTNKLFEENGIKVHRIPSSELSRGRGGPRCM  400
BORADIAFZ  GANVLAIAPGEIIAYSRNHVTNKLFEENGIKVHRIPSSELSRGRGGPRCM  400

BORADIBUR  SMSLVREDI  409
BORADIAFZ  SMPLIREDI  409
```

BORADIBUR = *Borrelia burgdorferi*

BORADIAFZ = *Borrelia afzellii*

FIG. 11

The alignment was done on 3 amino acid sequences.

Alignment

```
QIAADIINT   MTDFSKDKEKLAQATQGGENERAEIVVVHLPQGTSFLTSLNPEGNLLEEP   50
CLOADIPER   MRDDRALNVTSEIGRLKTVLLHRPGEEIENLTPDLLDRLLFDDIPYLKVA   50
BACADILIC   MIMTTPIHVYSEIGPLKTVMLKRPGRELENLTPEYLERLLFDDIPFLPAV   50

QIAADIINT   ICPDELRRDHEGFQAVLKEKGCRVYMPYDVLSEASPAEREVLMDQAMASL   100
CLOADIPER   REEHDAFAQTLREAGVEVLYLEVLAAEAIETSDEVKQQFISEFIDEAGVE   100
BACADILIC   QKEHDQFAETLKQQGAEVLYLEKLTAEALDDALVREQFIDELLTESKADI   100

QIAADIINT   KYELHATGARITPKMKYCVSDEYKRKVLSALSTRNLVDVILSEPVIHLAP   150
CLOADIPER   SERLKEALIEYFNSFSDNKAMVDKMMAGVRKEELKDYHRESLYDQVNNVY   150
BACADILIC   NGAYDRLKEFLLTFDADSMVEQVMSGIRKNELEREKKSHLHELMEDHYPF   150

QIAADIINT   GVRNTALVTNSVEIHDSNNMVFMRDQQITTRRGIVMGQFQAPQRRREQVL   200
CLOADIPER   PFVCDPMPNLYFTREPFATIGHGITLNHMRTDTRNRETIFAKYIFRHHPR   200
BACADILIC   YLDPMPNLYFTRDPAAAIGSGLTINKMKEPARRRESLFMRYIINHHPRFK   200

QIAADIINT   ALIFWKRLGARVVGDCREGGPHCMLEGGDFVPVSPGLAMMGVGLRSTYVG   250
CLOADIPER   FEGKDIPFWFNRNDKTSLEGGDELILSKEILAVGISQRTDSASVEKLAKK   250
BACADILIC   GHEIPVWLDRDFKFNIEGGDELVLNEETVAIGVSERTTAQAIERLVRNLF   250

QIAADIINT   AQYLMSKDLLGTRRFAVVKDCFDQHQDRMHLDCTFSVLHDKLVVLDDYIC   300
CLOADIPER   LLYYPDTSFKTVLAFKIPVSRAFMHLDTVFTQVDYDKFTVHPGIVGPLEV   300
BACADILIC   QRQSRIRRVLAVEIPKSRAFMHLDTVFTMVDRDQFTIHPAIQGPEGDMRI   300

QIAADIINT   SGMGLRYVDEWIDVGADAVKKAKSSAVTCGNYVLAKANVEFQQWLSENGY   350
CLOADIPER   YALTKDPENDGQLLVTEEVDTLENILKKYLDRDIKLIKCGGGDEIIAARE   350
BACADILIC   FVLERGKTADEIHTTEEHNLPEVLKRTLGLSDVNLIFCGGGDEIASAREQ   350

QIAADIINT   TIVRIPHEYQLAYGCNNLNLGNNCVLSVHQPTVDFIKADPAYISYCKSNN   400
CLOADIPER   QWNDGSNTLAIAPGEVVVYSRNYVTNEILEKEGIKLHVIPSSELSRGRGG   400
BACADILIC   WNDGSNTLAIAPGVVVTYDRNYISNECLREQGIKVIEIPSGELSRGRGGP   400

QIAADIINT   LPNGLDLVYVPFRGITRMYGSLHCASQVVYRTPLAPAAVKACEQEGDGIA   450
CLOADIPER   PRCMSMPLIREDL                                       413
BACADILIC   RCMSMPLYREDVK                                       413

QIAADIINT   AIYEKNGEPVDAAGKKFDCVIYIPSSVDDLIDGLKINLRDDAAPSREIIA   500

QIAADIINT   DAYGLYQKLVSEGRVPYITWRMPSMPVVSLKGAAKAGSLKAVLDKIPQLT   550

QIAADIINT   PFTPKAVEGAPAAYTRYLGLEQADICVDIK                       580
```

QIAADIINT = *Qiardia intestinalis*
CLOADIPER = *Clostridium perfringens*
BACADILIC = *Bacillus licheniformis*

FIG. 12

The alignment was done on 2 amino acid sequences.

Alignment

```
ENTADIFAE  MSHPINVFSEIGKLKTVMLHRPGKELENLMPDYLERLLFDDIPFLEKAQA   50
LACADISAK MTSPIHVNSEIGKLKTVLLKRPGKEVENITPDIMYRLLFDDIPYLPTIQK   50

ENTADIFAE  EHDAFAELLRSKDIEVVYLEDLAAEALINEEVRRQFIDQFLEEANIRSES  100
LACADISAK  EHDQFAQTLRDNGVEVLYLENLAAEAIDAGDVKEAFLDKMLNESHIKSPQ  100

ENTADIFAE  AKEKVRELMLEIDDNEELIQKAIAGIQKQELPKYEQEFLTDMVEADYPFI  150
LACADISAK  VQAALKDYLISMATLDMVEKIMAGVRTNEIDIKSKALIDVSADDDYPFYM  150

ENTADIFAE  IDPMPNLYFTRDNFATMGHGISLNHMYSVTRQRETIFGQYIFDYHPRFAG  200
LACADISAK  DPMPNLYFTRDPAASMGDGLTINKMTFEARQRESMFMEVIMQHHPRFANQ  200

ENTADIFAE  KEVPRVYDRSESTRIEGGDELILSKEVVAIGISQRTDAASIEKIARNIFE  250
LACADISAK  GAQVWRDRDHIDRMEGGDELILSDKVLAIGISQRTSAQSIEELAKVLFAN  250

ENTADIFAE  QKLGFKNILAFDIGEHRKFMHLDTVFTMIDYDKFTIHPEIEGGLVVYSIT  300
LACADISAK  HSGFEKILAIKIPHKHAMMHLDTVFTMIDYDKFTIHPGIQGAGGMVDTYI  300

ENTADIFAE  EKADGDIQITKEKDTLDNILCKYLHLDNVQLIRCGAGNLTAAAREQWNDG  350
LACADISAK  LEPGNNDEIKITHQTDLEKVLRDALEVPELTLIPCGGGDAVVAPREQWND  350

ENTADIFAE  SNTLAIAPGEVVVYDRNTITNKALEEAGVKLNYIPGSELVRGRGGPRCMS  400
LACADISAK  GSNTLAIAPGVVVTYDRNYVSNENLRQYGIKVIEVPSSELSRGRGGPRCM  400

ENTADIFAE  MPLYREDL                                           408
LACADISAK  SMPLVRRKT                                          409
```

ENTADIFAE = *Enterococcus faecalis*

LACADISAK = *Lactobacillus sake*

FIG. 13