

FIG. 1A
Nf1_{col2}^{-/-} Osteoblasts Secrete Increased Levels of Pyrophosphate (PP_i)

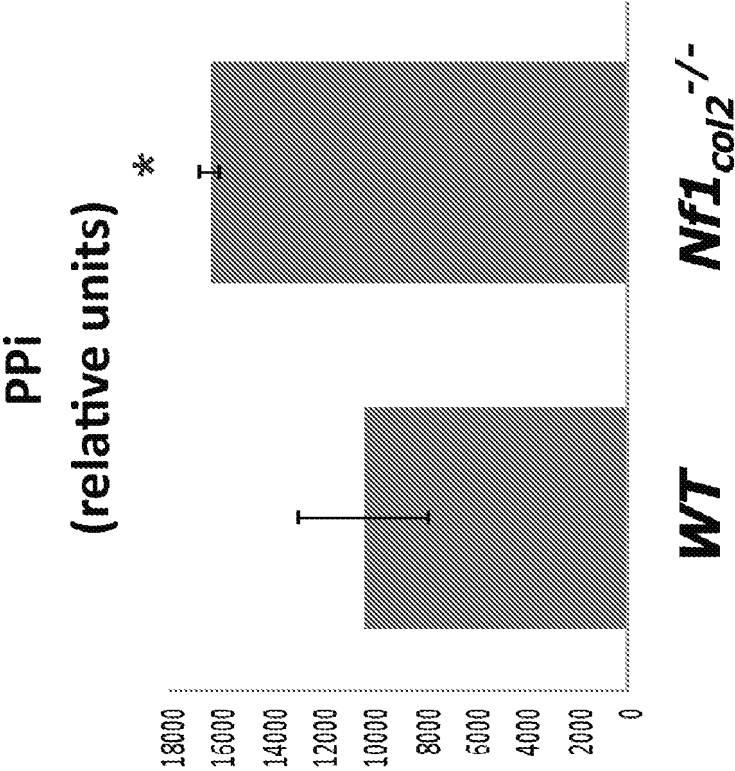


FIG. 1B
Increased *Ank* Expression in *Nf1*_{col2}^{-/-} Osteoblasts

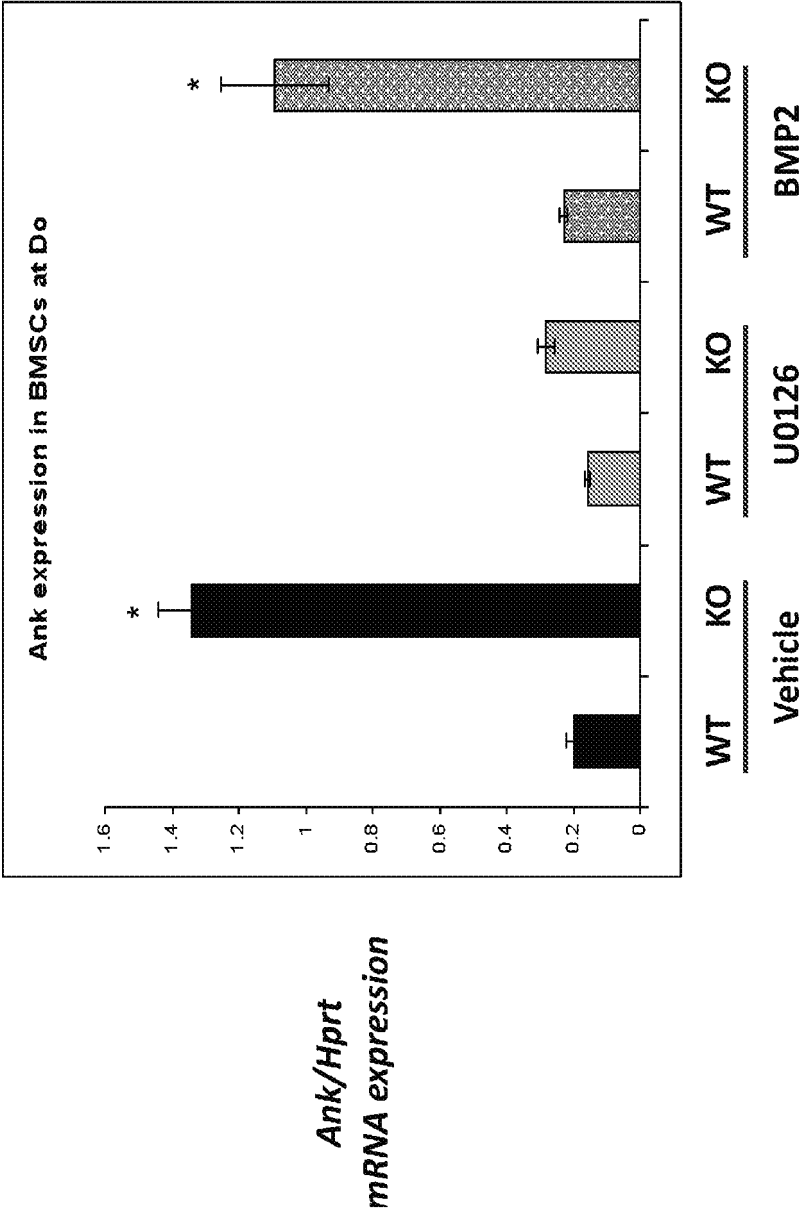
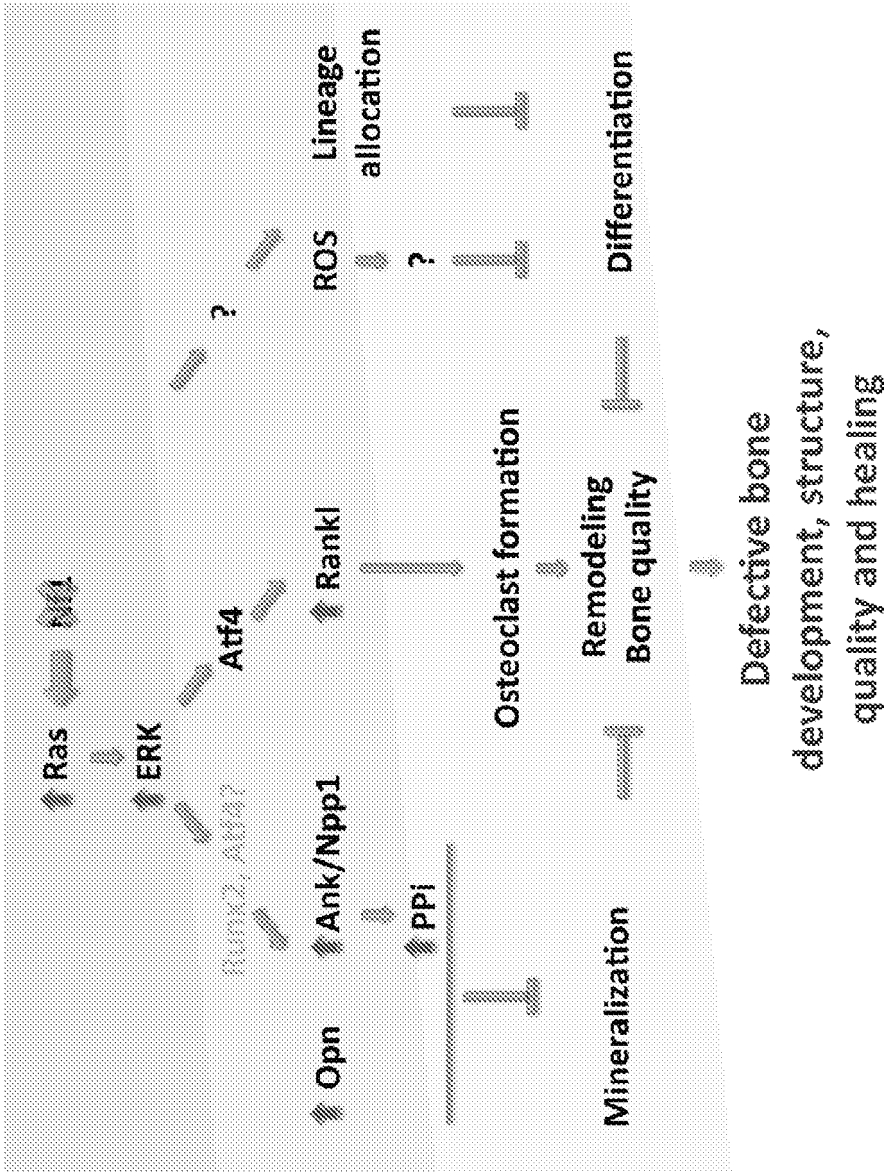


FIG. 2
Hypothetical Working Model for Defective Bone Matrix Mineralization in NF1_{col2}^{-/-} Mice



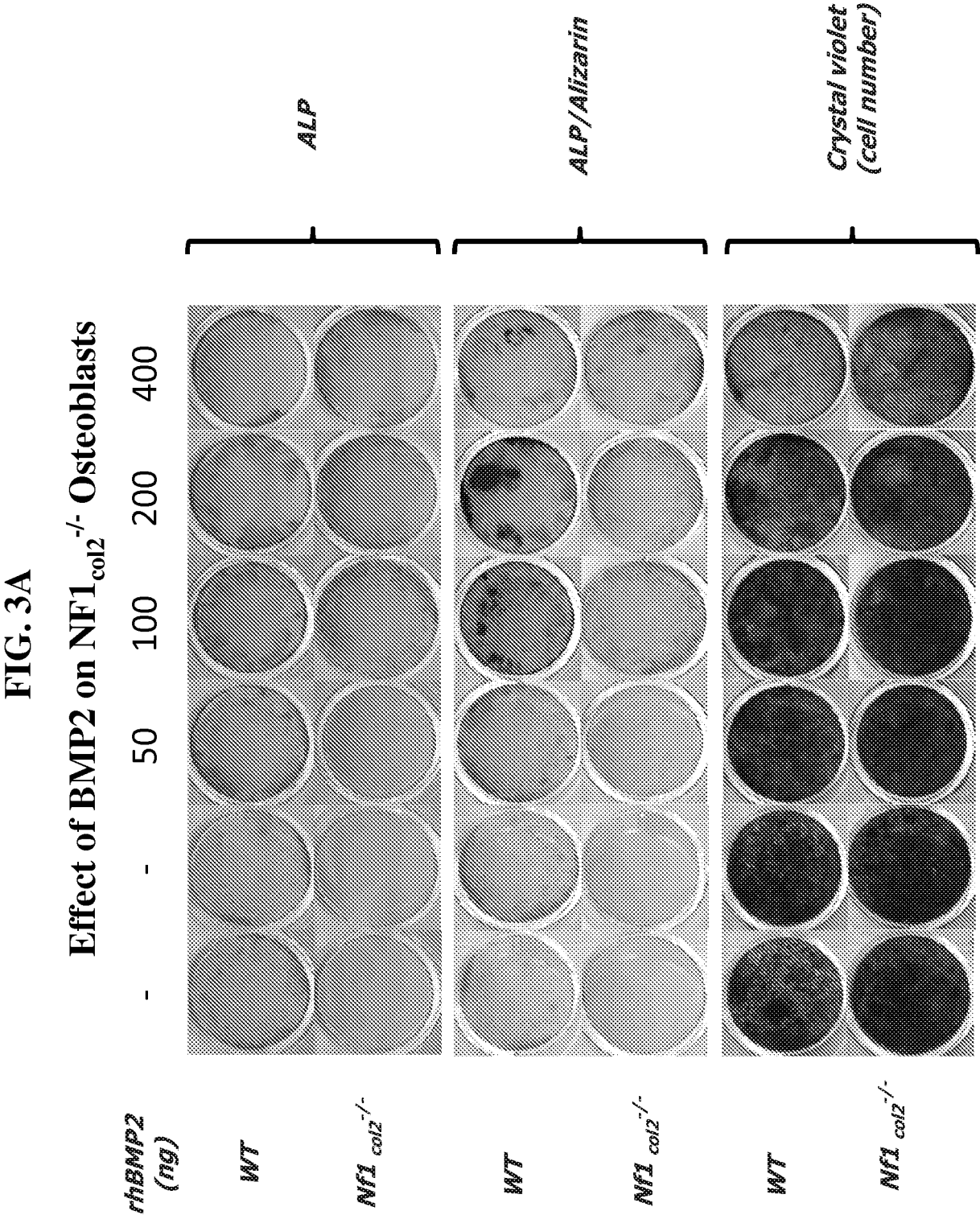


FIG. 3B

Effect of sTNALP-FcD₁₀ on Nf1^{col2}^{-/-} Bone Marrow Stromal Cells

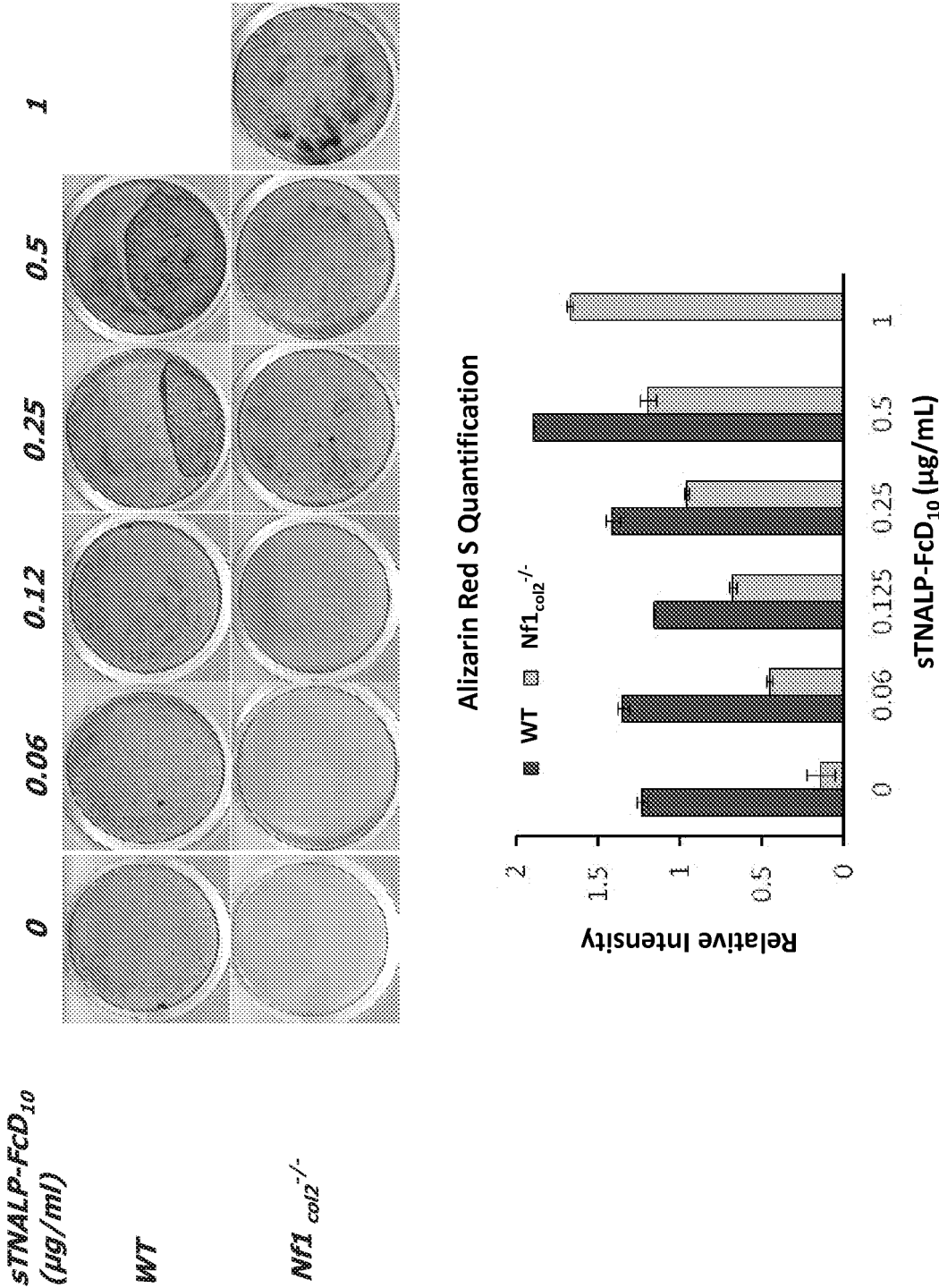


FIG. 3C
Effect of sTNALP-FcD₁₀ on NF1_{col2}^{-/-} Bone Marrow Stromal Cells

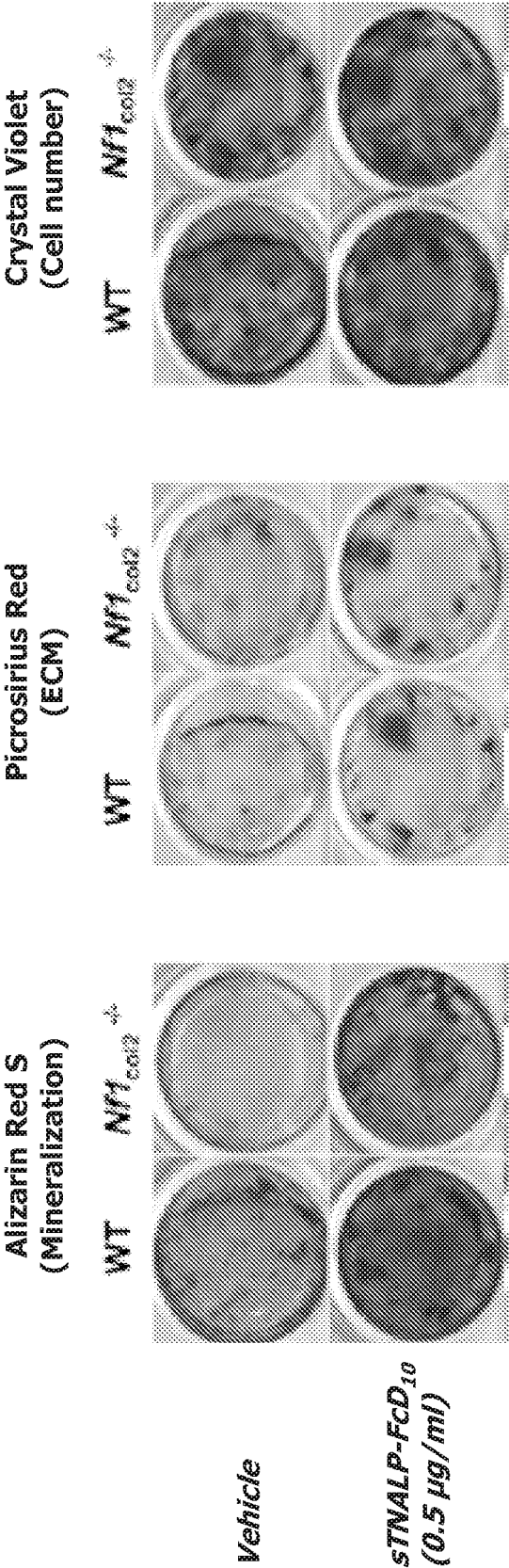


FIG. 3D
Effect of sTNALP-FcD₁₀ on Floxed NF1_{col2}^{-/-} Bone Marrow Stromal Cells

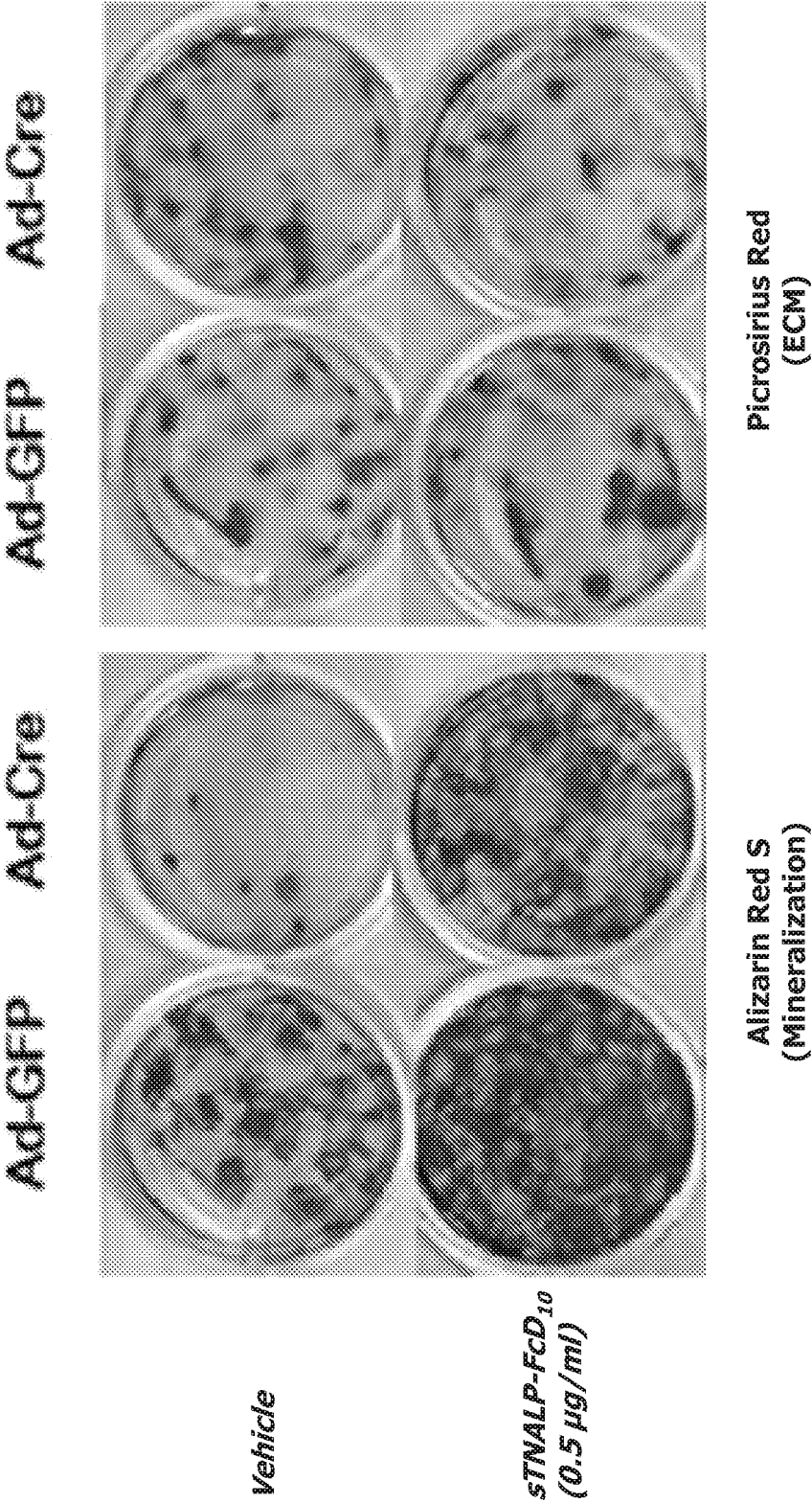


FIG. 3E
Effect of sTNALP-FcD₁₀ on Bone Volume in NF1_{col2}^{-/-} Mice

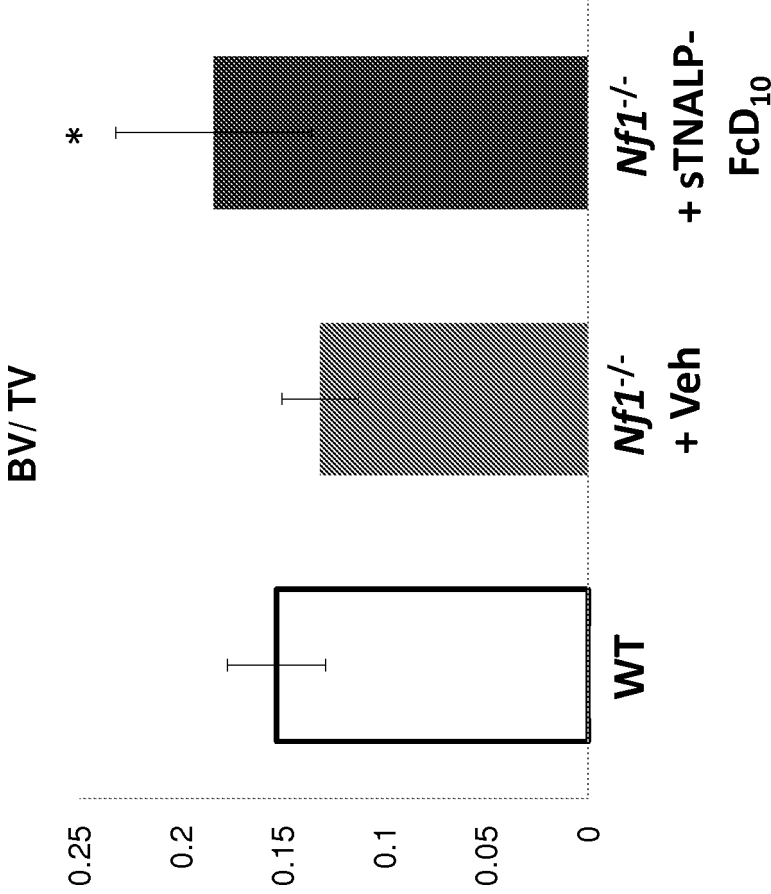
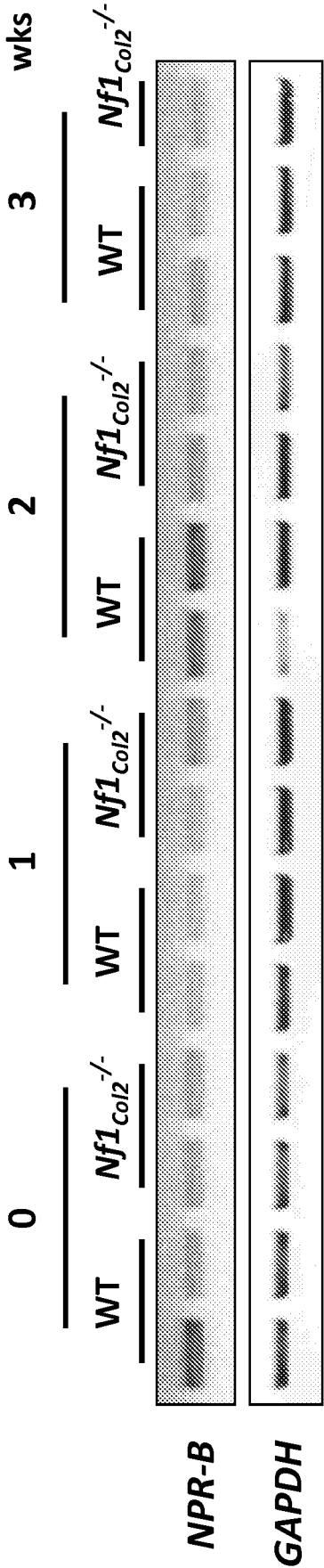
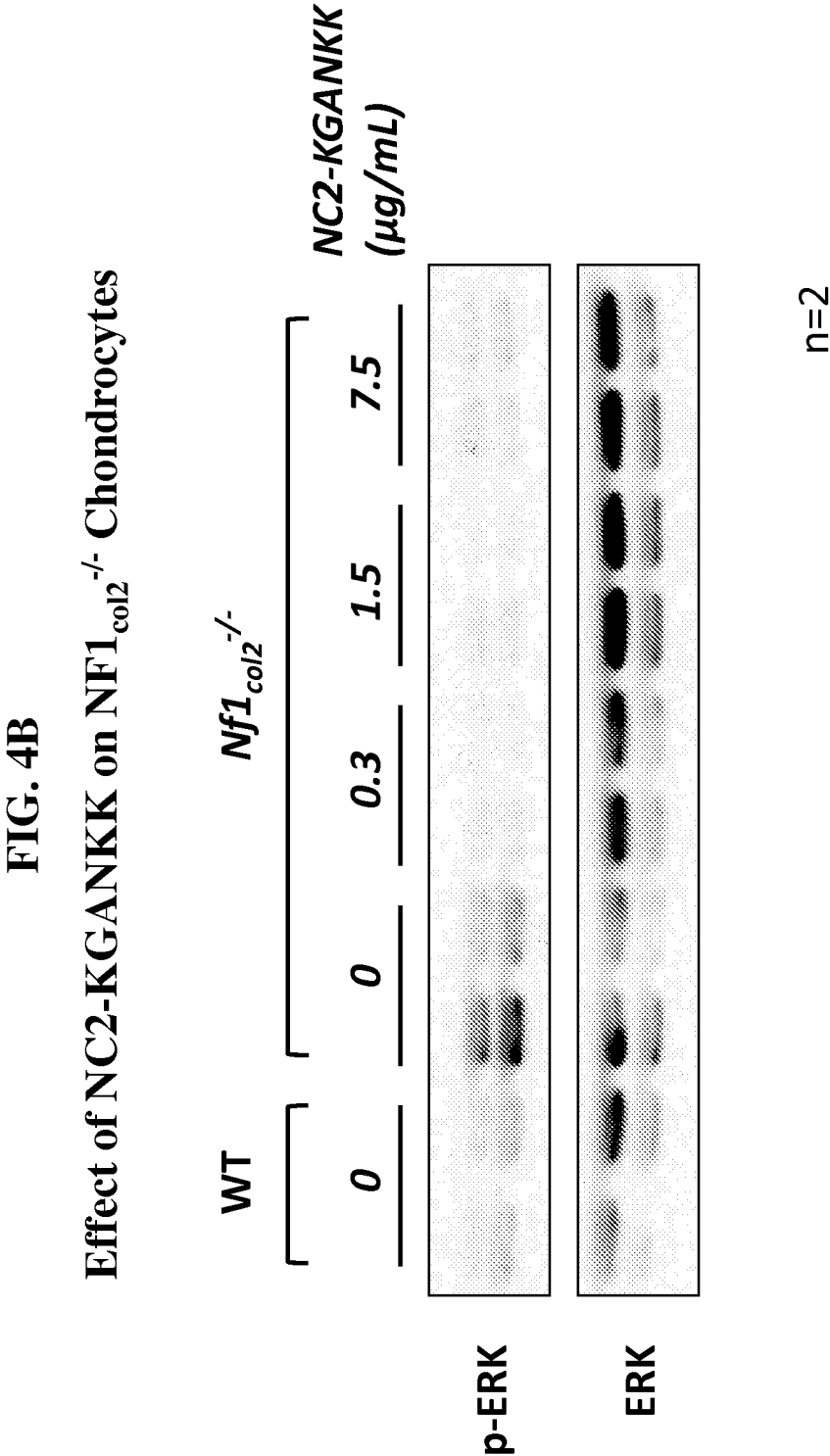


FIG. 4A
Expression of *NPR-B* Gene in *Nf1_{Col2}^{-/-}* Mice





P0 mice rib primary chondrocytes

FIG. 4C
Effect of NC2B on Naso-anal Length in $Nf1_{col2}^{-/-}$ Mice

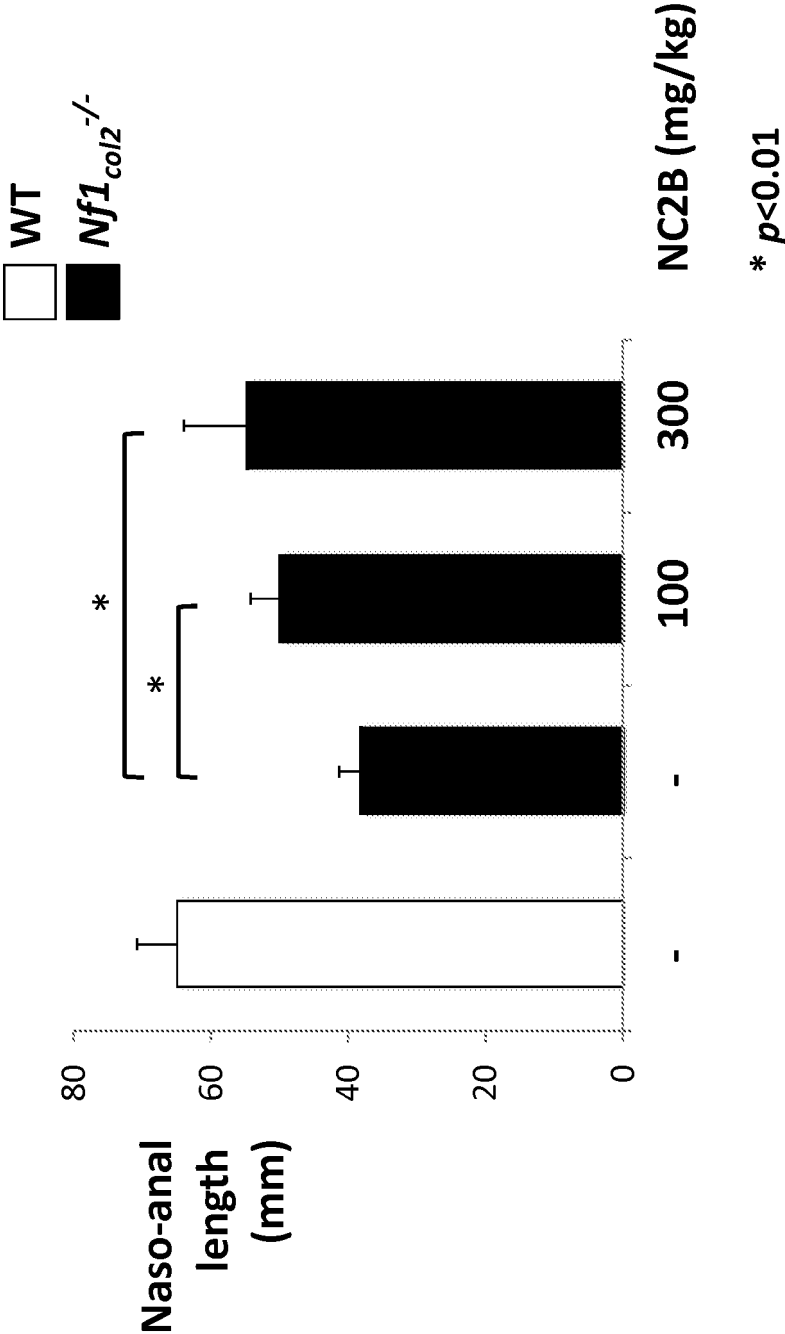


FIG. 4D
Effect of NC2B on Tibia Length in $Nf1_{col2}^{-/-}$ Mice

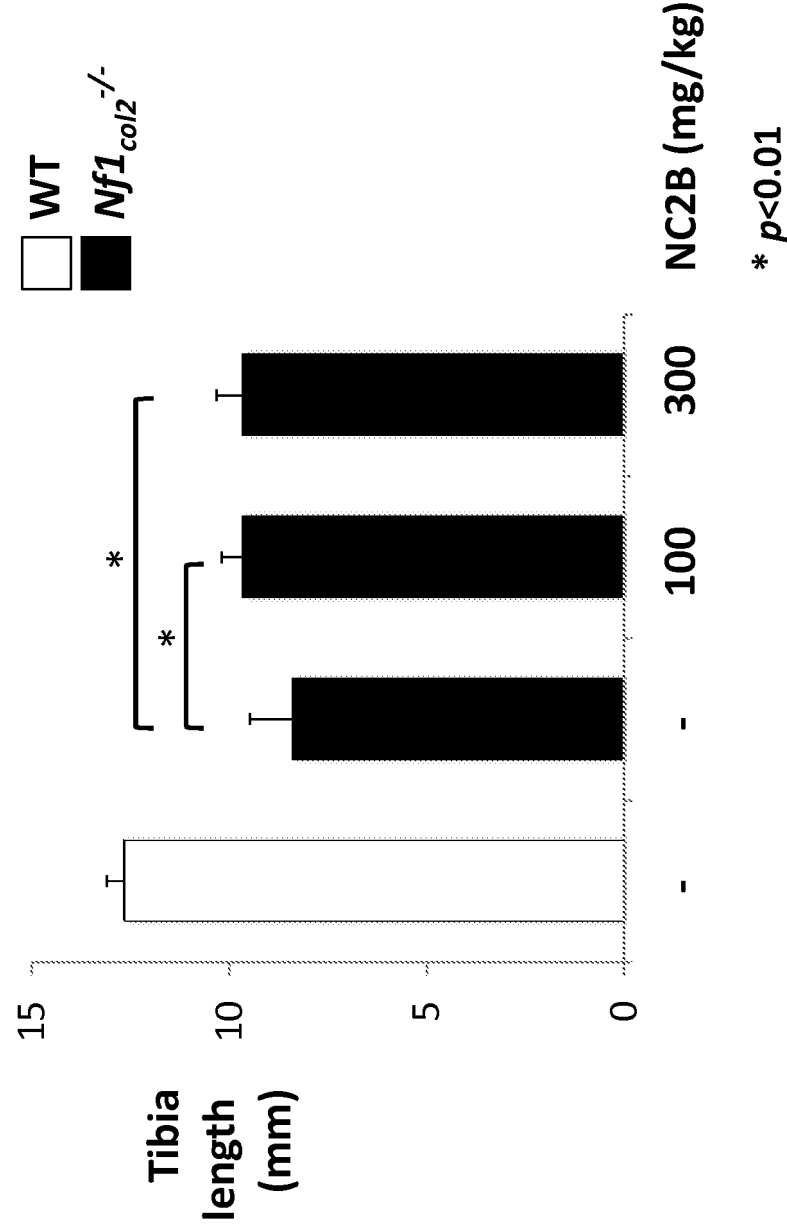


FIG. 4E
Effect of NC2B on Growth Plates in $Nf1_{col2}^{-/-}$ Mice

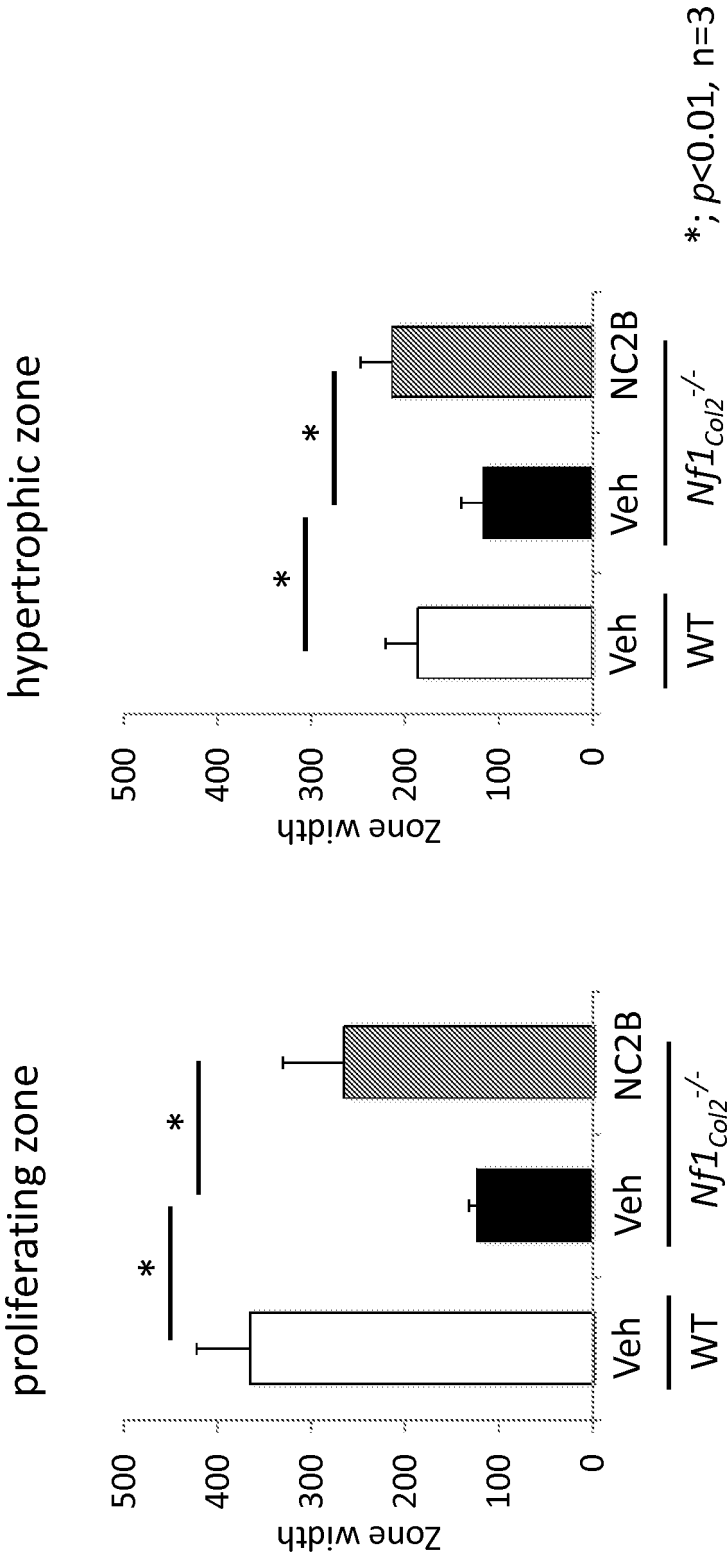


FIG. 5A
Schematic Structure of TNALP and hsTNALP-FcD₁₀
(With and Without Signal Sequence)

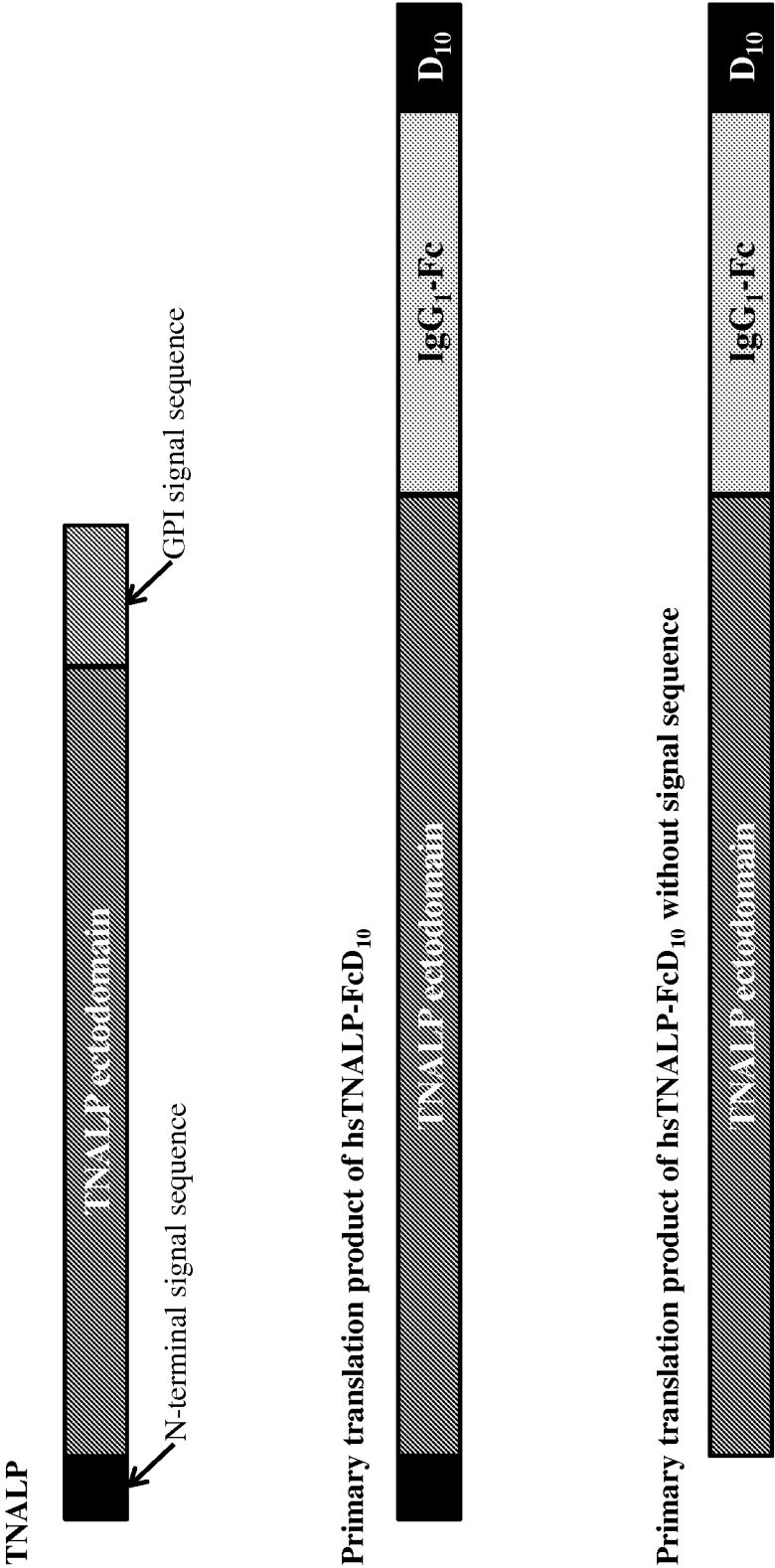


FIG. 5B
hsTNALP-FcD₁₀ Protein Sequence
(With and Without Signal Sequence)

sTNALP-FcD ₁₀ (w/sig. seq.)	MVSPFLVLAIGTCLTNSLVPEKEKDPKYWRDQAQETLKYLELQKLTNVAKNVMFLGDMGVSTVTAA RILKGQLHHNPGEETRLEMDKFFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCN TTQGNEVTSILRWAKDAGKSVGIVTTTRVNHATPSAAYAHSADRDWYSDNEMPPEALSQGCKDIAYQLMH NIRDIDVIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKHSHFINWRTELLTLDP HNVDYLLGLFEFGDMQYELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALH EAVEMDRAIGQAGSLTSSEDTLTVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGP YKVVGGERENVSMVDYAHNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACI GANLGHCAPASSLKDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSR WQQGNVFSSCSVMHEALHNHYTQKSLSLSPGKDIDDDDDDDDDD (SEQ ID NO: 1201)
sTNALP-FcD ₁₀ (w/o sig. seq.)	LVPEKEKDPKYWRDQAQETLKYLELQKLTNVAKNVMFLGDMGVSTVTAARILKGQLHHNPGEETRL EMDKFFPVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQGNEVTSILRWAKDA GKSVGIVTTTRVNHATPSAAYAHSADRDWYSDNEMPPEALSQGCKDIAYQLMHNIRDIDVIMGGGRKMY PKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKHSHFINWRTELLTLDPPHNVDYLLGLFEFGDMQY ELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIGQAGS LTS SEDTLTVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGPYKVVGGERENVSMVDYA HNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACIGANLGHCAPASSLKDKT HTCPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSRWQQGNVFSSCSVMHEALH NHYTQKSLSLSPGKDIDDDDDDDDDD (SEQ ID NO: 1204)

FIG. 5C
hsTNALP-Fc Protein Sequence
(With and Without Signal Sequence)

sTNALP-Fc (w/sig. seq.)	MVSPFLVLAIGTCLTNSLVPEKEKDPKYWRDQAQETLKYALELQKLTNTNVAKNVIMFLGDMGVSTVTAA RILKGQLHHNPGEETRLEMDKFFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCN TTQGNEVTSILRWAKDAGKSVGIVTTTRVNHATPSAAYAHSADRDWYSDNEMPEALSQGCKDIAYQLMH NIRDIDVIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKHSHFIWNRTELLTLDP HNVDYLLGLFEFGDMQYELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALH EAVEMDRAIGQAGSLTSSEDTLTVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGP YKVVGGERENVSMVDYAHNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACI GANLGHCAPASSLDKTKHTCPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSR WQQGNVFSSCSVMHEALHNHYTQKSLSSPGK (SEQ ID NO: 1220)
sTNALP-Fc (w/o sig. seq.)	LVPEKEKDPKYWRDQAQETLKYALELQKLTNTNVAKNVIMFLGDMGVSTVTAARILKGQLHHNPGEETRL EMDKFFPVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQGNEVTSILRWAKDA GKSVGIVTTTRVNHATPSAAYAHSADRDWYSDNEMPEALSQGCKDIAYQLMHNIRDIDVIMGGGRKMY PKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKHSHFIWNRTELLTLDPPHNVDYLLGLFEFGDMQY ELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIGQAGSLT SEDTLTVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGPYKVVGGERENVSMVDYA HNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACIGANLGHCAPASSLDKTKT HTCPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYTLPPSREEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSRWQQGNVFSSCSVMHEALH NHYTQKSLSLSPGK (SEQ ID NO: 1221)

FIG. 5D

hsTNALP-FcD₁₀ DNA Sequence

atgggtttcac cattcttagt actggccatt ggcacctgcc ttactaactc cttagtgcca gagaaagaga aagacccccaa gtactggcga
 gaccaagcgc aagagacact gaaatatgcc ctggagcttc agaagctcaa caccacactg gctaagaatg tcatcatgtt cctgggagat
 gggatgggtg tctccacagt gacggtgcc cgcacctca aggttcagct ccaccacaac cctggggagg agaccaggct ggagatggac
 aagttcccc tegtggccct ctccaagacg tacaacacca atgcccagggt cctgacagc gccggcaccg ccaccgccta cctgtgtggg
 gtgaaggcca atgagggcac cgtggggta agcgcagcca ctgagcgttc ccggtgcaac accaccagg ggaacgaggt cacctccatc
 ctgcgtggg ccaaggacgc tgggaaatct gtggcattg tgaccaccac gagagtgaac catgccacc catcgccgc ctacgcccac
 tcggctgacc gggactggtg ctacagacaac gagatgcccc ctgaggcctt gagccaggc tgtaaggaca tgcctacca gctcatgcat
 aacatcaggg acattgacgt gatcatggg ggtggccgga aatacatgta cccaagaat aaaactgatg tggagtatga gagtgcagag
 aaagccaggg gcacgaggct ggacggcctg gacctcgtt acacctggaa gagcttcaaa ccgagataca agcactccca ctcatctgg
 aacgcacgg aactcctgac ccttgacccc cacaatgtgg actacctatt ggtctcttc gagccagggt acatgcagta cgagctgaac
 aggaacaacg tgacggaccc gtcactctcc gagatggtgg tggtggccat ccagatcctg cggaagaacc ccaaaggctt ctcttgctg
 gtggaaggag gcagaattga ccacgggcac catgaaggaa aagccaagca ggccctgcat gaggcgttg agatggaccg ggccatcggg
 caggcaggca gcttgacctc ctcggaagac actctgaccg tggtcactgc ggaccattcc cactcttca catttggtgg atacacccc
 cgtggcaact ctatctttgg tctggcccc atgctgagt acacagaaa gaagcccttc actgccatcc tgtaggcaa tgggcctggc
 tacaaggtg tggcggtga acgagagaat gtctccatgg tgactatgc tcaacaacac taccagggc agtctgctgt gccctgcgc
 cacgagacc acggcgggga ggaactggcc gtcttctca agggcccat ggcgacctg ctgcacggcg tccacgagca gaactacgtc
 cccacagtga tggcgatgc agcctgcac ggggccaacc tcggccactg tgctcctgcc agctcgtTA AGgacaaaac tcacacatgc
 ccacogtgc cagcacctga actcctggg ggaactcag tcttctctt cccccaaaa cccaaggaca cctcatgat ctcccgacc
 cctgaggtca catgcgtggt ggtggactg agccacgaag accctgaggt caagttcaac tggtaactgg acggcgtgga ggtgcataat
 gccaaagaca agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtctc cagcgtctgc accaggactg gctgaatggc
 aaggagtaca agtgcaaggt ctccaacaaa gccctccag ccccatcga gaaaaccatc tccaaagca aagggcagcc ccgagaacca
 caggtgtaca cctgcccc atccccggg gagatgacca agaaccaggt cagcctgacc cagcgttca aaggttcta tccagcgac
 atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc gtgtgact ccgacggctc ctcttctc
 tatagcaagc tcaccgtgga caagagcagg tggcagcagg ggaactcct ctcatgctcc gtgatgcagt aggtctctgca caaccactac
 acgcagaaga gcctctccct gtctccgggt aaagATATCG ATGACGATGA CGATGACGAT GACGATGACT AG (SEQ ID NO: 1217)

FIG. 6
Human Soluble Tissue Nonspecific Alkaline Phosphatase
(hsTNALP) Protein Sequence

hsTNALP (1-502)	<u>MVSPFLVLAIGTCLTNSL</u> VPKEKDPKYWRDQAQETLK YALELQKLNTN VAKNVI MF LGDMGVSTVTAARI LK Q LHHNPGEETRLEMDKFPFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQG NEVTSILRWAKDAGKSVGIVTTTRVNHATPSAAYAH SADRDW YSDNEMPPEALSQGCKDIA YQ LMHNIRDID VIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRT ELLTLD PHNV VDYLLG LFEPGDMQYELNRRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIG QAGSLTSS EDTLTV VIADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYNGNGPGYKVVGGERENV MVDYAHNNYQAQSAVPLR HETHGGED VAVFSKGPMAHLLHGVHEQNYVPHVMAYAAACIGANLGHCAPASS (SEQ ID NO: 1202)
hsTNALP (18-502)	LVPEKEKDPKYWRDQAQETLK YALELQKLNTN VAKNVI MF LGDMGVSTVTAARILK Q LHHNPGEETRLEM DKFPFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQ NEVTSIL RWAKDAGKSV GIVTTTRVNHATPSAAYAH SADRDW YSDNEMPPEALSQGCKDIA YQ LMHNIRDIDVIMGGGRKYMYPKNKTD VEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRT ELLTLD PHNV VDYLLG LEPDMQYELNRRNNVT DPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIGQAGSLTSS EDTLTV VI ADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYNGNGPGYKVVGGERENVSMVDYAHNNYQAQSAVPL R HETHGGED VAVFSKGPMAHLLHGVHEQNYVPHVMAYAAACIGANLGHCAPASS (SEQ ID NO: 1205)

FIG. 7
Exemplary Fc Sequence (IgG-1)

DKTHTCPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV
DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 401)

FIG. 8

Multiple Sequence Alignment of Tissue Nonspecific Alkaline Phosphatase (TNALP)

CLUSTAL W (1.82) multiple sequence alignment: Tissue Nonspecific Alkaline Phosphatase

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1  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  Q29486|PPBT_BOVIN  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  Q29486|PPBT_FELCA  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  P05186|PPBT_HUMAN  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  P09242|PPBT_MOUSE  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  P08289|PPBT_RAT  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  Q9N0V0|Q9N0V0_CANFA  MISPFLLAI  GTCFASSLVP  EKEKDPKYMR  DQAQOTLKNA  LRLQTLNTNV  AKNVIMFLGD
  -----
  XXXXXXXXXXXX  XXXXXXXXXXXX  XXEXDPXYMR  XQAQXTLKXA  LXQLXLTNV  XKNXIMFLGD
  Consensus

61  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  Q29486|PPBT_BOVIN  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  Q29486|PPBT_FELCA  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  P05186|PPBT_HUMAN  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  P09242|PPBT_MOUSE  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  P08289|PPBT_RAT  GMGVSTVTAA  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  Q9N0V0|Q9N0V0_CANFA  GMGVSTVTAT  RILKGQLHHS  PGEETKLEMD  KFPYVALSKT  YNTNAQVPDS  AGTATAYLCC
  *****
  GMGVSTVTAX  RILKGQLHHS  XGEETXLEMD  KFPXVALSKT  YNTNAQVPDS  AGTATAYLCC
  Consensus

121  VKANEGTVGV  SAATQRSQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSASYAH
  Q29486|PPBT_BOVIN  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  Q29486|PPBT_FELCA  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  P05186|PPBT_HUMAN  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  P09242|PPBT_MOUSE  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  P08289|PPBT_RAT  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  Q9N0V0|Q9N0V0_CANFA  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  *****
  VKANEGTVGV  SAATQRTQC  TTQGNEVTSI  LRWAKDAGKS  VGIVTTTRVN  HATPSAAYAH
  Consensus

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FIG. 8 (cont'd)

181	P09487 PPBT_BOVIN	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMY	NIKDIEVIMG	GGRKYMFPKN	RTDVEYELDE
	Q29486 PPBT_FELCA	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NVRDIEVIMG	GGRKYMFPKN	RTDVEYEMDE
	P05186 PPBT_HUMAN	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIRDIDVIMG	GGRKYMFPKN	KTDVEYESDE
	P09242 PPBT_MOUSE	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIKDIDVIMG	GGRKYMFPKN	RTDVEYELDE
	P08289 PPBT_RAT	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIKDIDVIMG	GGRKYMFPKN	RTDVEYELDE
	Q9N0V0 Q9N0V0_CANFA	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NVKDIEVIMG	GGRKYMFPKN	RTDVEYEMDE
	Consensus	*****	*****	*****	*:****	*****:***	:***** **
		SADRDWYSDN	EMPPEALSQG	CKDIAYQLMX	NXXDIXVIMG	GGRKYMFPKN	XTDVEYEXDE
241	P09487 PPBT_BOVIN	KARGTRLDGL	NLIDIWKSFK	PKHKHSHYVW	NRTDLLALDP	HSVDYLLGLF	EPGDMQYELN
	Q29486 PPBT_FELCA	KARGTRLDGL	NLVDIWKSFK	PRHKHSHYVW	NRTELLTLDP	YGVDYLLGLF	EPGDMQYELN
	P05186 PPBT_HUMAN	KARGTRLDGL	DLVDTWKSFK	PRYKHSFIW	NRTELLTLDP	HNVDYLLGLF	EPGDMQYELN
	P09242 PPBT_MOUSE	KARGTRLDGL	DLISIWKSFK	PRHKHSHYVW	NRTELLALDP	SRVDYLLGLF	EPGDMQYELN
	P08289 PPBT_RAT	KARGTRLDGL	DLISIWKSFK	PRHKHSHYVW	NRTELLALDP	SRVDYLLGLF	EPGDMQYELN
	Q9N0V0 Q9N0V0_CANFA	KSTGARLDGL	NLIDIWKNFK	PRHKHSHYVW	NRTELLALDP	YFVDYLLGLF	DPGDMQYELN
	Consensus	*:*****	:*:. **.*	*:*****:*	***:***	*****	:*****
		KXXGXRLDGL	XLXXXWXXFK	PXXKHSXXXW	NRTXLLXLDP	XXVDYLLGLF	XPGDMQYELN
301	P09487 PPBT_BOVIN	RNNATDPSLS	EMVEMAIRIL	NKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	Q29486 PPBT_FELCA	RNSTTDPSLS	EMVEIAIKIL	SKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	P05186 PPBT_HUMAN	RNNVTDPSLS	EMVVAIQIL	RKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDRAIG
	P09242 PPBT_MOUSE	RNNLTDPSLS	EMVEVALRIL	TKNLKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	P08289 PPBT_RAT	RNNLTDPSLS	EMVEVALRIL	TKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDEAIG
	Q9N0V0 Q9N0V0_CANFA	RNNVTDPSLS	EMVEIAIKIL	SKKPRGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDRAIG
	Consensus	** *****	***:***	*:*****	*****	*****	:*****
		RNXXTDPSLS	EMVXXAXXIL	XXXXXGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDXAIG

FIG. 9

Multiple Sequence Alignment of Alkaline Phosphatase
(TNALP, GALP, PLALP, and IALP)

CLUSTAL 2.0.5 multiple sequence alignment									
TNALPrn	MILP-----F	LVLAIGTCLT	NSFVPEKEKD	PSYWRQQAQE	TKNALKLQK	LNTNVAKNII	55		
TNALPmm	MISP-----F	LVLAIGTCLT	NSFVPEKERD	PSYWRQQAQE	TKNALKLQK	LNTNVAKNVI	55		
TNALPhs	MISP-----F	LVLAIGTCLT	NSLVPEKEKD	PKYWRDQAQE	TKYALELQK	LNTNVAKNVI	55		
TNALPcf	-----	-----	-----EKD	PKYWRDQAQQ	TKYALRLQN	LNTNVAKNVI	33		
TNALPfc	MISP-----F	LVLAIGTCLT	NSLVPEKEKD	PKYWRDQAQQ	TKNALRLQK	LNTNVVKNVI	55		
TNALPbt	MISP-----F	LLLAIGTCFA	SSLVPEKEKD	PKYWRDQAQQ	TKNALRLQT	LNTNVAKNVI	55		
GALPhs	MQGPWV---L	LLGLRLQLS	LGIIPVEEEN	PDFWNRQAAE	ALGAAKKLQP	AQT-AAKNLI	56		
PLALPhs	MLGPCMLLLL	LLGLRLQLS	LGIIPVEEEN	PDFWNRQAAE	ALGAAKKLQP	AQT-AAKNLI	59		
IALPhs	MQGPWV---L	LLGLRLQLS	LGVTPAFEEEN	PAFWNRQAAE	ALDAAKKLQP	IQK-VAKNLI	56		
Consensus	XXXXXXXXXX	XXXXXXXXXX	*.: * :*. :* : * : * : * : * : *	XXXXXXXAXX	XXXXXXXXLQX	XXXXXXXXKXI			
TNALPrn	MFLGDGMGVS	TVTAARILKG	QLHNTGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPmm	MFLGDGMGVS	TVTAARILKG	QLHNTGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPhs	MFLGDGMGVS	TVTAARILKG	QLHNPGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPcf	MFLGDGMGVS	TVTATRILKG	QLHNPGEET	RLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	93		
TNALPfc	MFLGDGMGVS	TVTAARILKG	QLHNPGEET	RLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPbt	MFLGDGMGVS	TVTAARILKG	QLHSPGEET	KLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	115		
GALPhs	IFLGDGMGVS	TVTAARILKG	QKDKLGPET	FLAMDRFPYV	ALSKTYSVDK	HVPDSGATAT	116		
PLALPhs	IFLGDGMGVS	TVTAARILKG	QKDKLGPEI	PLAMDRFPYV	ALSKTYNVDR	HVPDSGATAT	119		
IALPhs	LFLGDGLGVP	TVTATRILKG	QKNGKLGPEI	PLAMDRFPYL	ALSKTYNVDR	QVPDSAAATAT	116		
Consensus	:*****:	*****	* :. * *	* **::**::	*****:	:*****:			
	XFLGDGXGVX	TVTAXRILKG	QXXXXXXGXEX	XLXMDXFPXX	ALSKTYXXXX	XVPDSXXTAT			

TNALPrn	AYLCGVKANE	GTVGVSAAE	RTRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPmm	AYLCGVKANE	GTVGVSAAE	RTRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPhs	AYLCGVKANE	GTVGVSAAE	RSRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPcf	AYLCGVKANE	GTVGVSAAQ	RTHCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	153
TNALPfc	AYLCGVKANE	GTVGVSAAQ	RTQCNTTQGN	EVTSILRWAK	DSGKSVGIVT	TTRVNHATPS	175
TNALPbt	AYLCGVKANE	GTVGVSAAQ	RSQCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
GALPhs	AYLCGVKGNF	QTIGLSAAAR	FNQCNTTTRGN	EVISVMNRK	KAGKSVGVT	TTRVQHASPA	176
PLALPhs	AYLCGVKGNF	QTIGLSAAAR	FNQCNTTTRGN	EVISVMNRK	KAGKSVGVT	TTRVQHASPA	179
IALPhs	AYLCGVKANF	QTIGLSAAAR	FNQCNTTTRGN	EVISVMNRK	QAGKSVGVT	TTRVQHASPA	176
	***** *	*****:	*****:	*****:	*****:	*****:	
Consensus	AYLCGVKXNX	XTXGXSAAXX	XXXCNTTXGN	EVXSSXXXAK	XXGKSVGXVT	TTRVXXHAXPX	
TNALPrn	AAAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKDI	DVIMGGGRKY	MYPKNRTDVE	235
TNALPmm	AAAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKDI	DVIMGGGRKY	MYPKNRTDVE	235
TNALPhs	AAAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMHNIRDI	DVIMGGGRKY	MYPKNKT DVE	235
TNALPcf	AAAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMHNVKDI	EVIMGGGRKY	MFPKNRTDVE	213
TNALPfc	AAAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMHNVRDI	EVIMGGGRKY	MFPKNRTDVE	235
TNALPbt	ASAYHSADR	WYSDNEMPPE	ALSQGCKDIA	YQLMYSNM-DI	EVIMGGGRKY	MFPKNRTDVE	235
GALPhs	GAYAHTVNRN	WYSDADVPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFPMGTPDPE	235
PLALPhs	GTYAHTVNRN	WYSDADVPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFPMGTPDPE	238
IALPhs	GTYAHTVNRN	WYSDADMPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFPMGTPDPE	235
	*****:	*****:	*****:	*****:	*****:	*****:	
Consensus	XXYAHXXXRX	WYSDXXXPPXX	AXXXGCXDIA	XQLXXNXXDI	XVIXGGGRKY	MXXXXXXXDDE	
TNALPrn	YELDEKARGT	RLDGLDLISI	WKSFKPRHKH	SHYVWNRTL	LALDPS-RVD	YLLGLFEPGD	294
TNALPmm	YELDEKARGT	RLDGLDLISI	WKSFKPRHKH	SHYVWNRTL	LALDPS-RVD	YLLGLFEPGD	294
TNALPhs	YESDEKARGT	RLDGLDLVDT	WKSFKPRYKH	SHFIWNRTL	LTLDPH-NVD	YLLGLFEPGD	294
TNALPcf	YEMDEKSTGA	RLDGLNLIDI	WKNFKPRHKH	SHYVWNRTL	LALDPY-TVD	YLLGLFDPGD	272
TNALPfc	YEMDEKARGT	RLDGLNLVDT	WKSFKPRHKH	SHYVWNRTL	LTLDPY-GVD	YLLGLFEPGD	294
TNALPbt	YELDEKARGT	RLDGLNLIDI	WKSFKPKHKH	SHYVWNRTDL	LALDPH-SVD	YLLGLFEPGD	294
GALPhs	YPDDYSQGGT	RLDGKNLVQE	WL---AKHQG	ARYVWNRTL	LQASLDPSVT	HLMGLFEPGD	292
PLALPhs	YPDDYSQGGT	RLDGKNLVQE	WL---AKRQG	ARYVWNRTL	MQASLDPSVT	HLMGLFEPGD	295
IALPhs	YPADASQNGI	RLDGKNLVQE	WL---AKHQG	AWYVWNRTL	MQASLDQSVT	HLMGLFEPGD	292
	* * *	**** *	* :	: :	: :	: :	
Consensus	YXXDXXXXGX	RLDGXXLXXX	WXXXXXXXXX	XXXXWNRTXL	XXXXXXXXXXV	XLXGLFXPGD	

FIG. 9 (cont'd)

TNALPrn	MQYELNRNLL	TDPSLSEMV	VALRILTKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPmm	MQYELNRNLL	TDPSLSEMV	VALRILTKNL	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPhs	MQYELNRNNV	TDPSLSEMV	VAIQILRKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPcf	MQYELNRNNV	TDPSLSEMV	IAIKILSKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	332
TNALPfc	MQYELNRNST	TDPSLSEMV	IAIKILSKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPbt	MQYELNRNNA	TDPSLSEMV	MAIRILNKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
GALPhs	MKYEIHRDST	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHESR	AYRALTETIM	352
PLALPhs	MKYEIHRDST	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHESR	AYRALTETIM	355
IALPhs	TKYEIHRDPT	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHEGV	AYQALTEAVM	352
	:***::	**** **	*: * ::	:***:****	*****	* : ** *::	
Consensus	XXYEXRXXX	XDPSLXEMXX	XAXXXLXXXX	XGFXLXVEGG	RIDGHGHEXX	AXXALXEXXX	
TNALPrn	MDEAIGKAGT	MTSQKDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
TNALPmm	MDQAIGKAGA	MTSQKDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
TNALPhs	MDRAIGQAGS	LTSSDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMLSD	TDKKPFTAIL	414
TNALPcf	MDRAIGKAGV	MTSLEDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	392
TNALPfc	MDQAIGRAGA	MTSVEDTLTI	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTSIL	414
TNALPbt	MDQAIGQAGA	MTSVEDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
GALPhs	FDDAIERAGQ	LTSEEDTSL	VTADHSHVFS	FGGYPLRGSS	IFGLAPGKAR	-DRKAYTVLL	411
PLALPhs	FDDAIERAGQ	LTSEEDTSL	VTADHSHVFS	FGGYPLRGSS	IFGLAPGKAR	-DRKAYTVLL	414
IALPhs	FDDAIERAGQ	LTSEEDTLTL	VTADHSHVFS	FGGYTLRGSS	IFGLAPSKAQ	-DSKAYTSIL	411
	:* ** : **	:** :****:	*****:	****.***	*****	* * : * : *	
Consensus	XDXAIXXAGX	XTSXXDTLXX	VTADHSHVFX	FGGYXXRGXS	IFGLAPXXXX	XDXXXTXXL	
TNALPrn	YNGPGYKVV	DGERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPmm	YNGPGYKVV	DGERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPhs	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFSK	GPMHLLHGV	474
TNALPcf	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	452
TNALPfc	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPbt	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
GALPhs	YNGPGYVLK	DGARDPVTE	ESGSPEYRQ	SAVPLDGETH	AGEDVAVFAR	GPQHLVHGV	471
PLALPhs	YNGPGYVLK	DGARDPVTE	ESGSPEYRQ	SAVPLDEETH	AGEDVAVFAR	GPQHLVHGV	474
IALPhs	YNGPGYVFN	SGVRPDVNES	ESGSPDYQQ	AAVPLSSETH	GGEDVAVFAR	GPQHLVHGV	471
	*****	. * * : *	: . : * :	:****	***	*****	** * : * : *
Consensus	YNGPGYXXX	XGXRXXVXXX	XXXXXXVXXX	XAVPLXXETH	XGEDVAVFXX	GPXAHXXHGV	

FIG. 9 (cont'd)

TNALPrn	HEQNYIPHV	AYASCIG---	-ANLDHC	AWA	SSASSP	SPGA	LLLPLA	LFPL	RTLF-----	524
TNALPmm	HEQNYIPHV	AYASCIG---	-ANLDHC	AWA	SGSAP	SPGA	LLLPLA	VL	PTLF-----	524
TNALPhs	HEQNYVPHV	AYAACIG---	-ANLGH	CAPA	SSAGS	LAAGP	LLLALA	LYPL	SVLF-----	524
TNALPcf	HEQNYIPHV	AYAACIG---	-ANQDH	CASA	SSAGG	SPSPG	LLLLLA	LLPV	GILF-----	502
TNALPfc	HEQNYIPHV	AYAACIG---	-ANLDH	CASA	SSAGG	SPSPG	LFLLLA	LLPSL	GILF-----	524
TNALPbt	QEQNYIPHV	AYAACIG---	-ANRDH	CASA	SSSGS	SPSPG	LLLLLA	LLPL	GSIF-----	524
GALPhs	QEQTFIGHV	AFACLEPYT	ACDLAP	PRAGT	TDAAH	PGPSV	VPALLP	LLAG	TLLLLGTATA	531
PLALPhs	QEQTFIGHV	AFACLEPYT	ACDLAP	PPAGT	TDAAH	PGRSV	VPALLP	LLAG	TLLLLETATA	534
IALPhs	QEQSFIGHV	AFACLEPYT	ACDLAP	PPACT	TDAAH	P----	VAASLP	LLAG	TLLLLGASAA	527
Consensus	:**...***	*:*:*:	::	*	:	...	:	*::	*	:
	XEQXXXXHV	AXAXCXXXXX	XXXXXX	AXX	XXXXXX	XXXXX	XXXXL	XXXXX	XXLXXXXXX	
TNALPrn	-	(SEQ ID NO: 1210)								
TNALPmm	-	(SEQ ID NO: 1209)								
TNALPhs	-	(SEQ ID NO: 1208)								
TNALPcf	-	(SEQ ID NO: 1211)								
TNALPfc	-	(SEQ ID NO: 1207)								
TNALPbt	-	(SEQ ID NO: 1206)								
GALPhs	P 532	(SEQ ID NO: 1213)								
PLALPhs	P 535	(SEQ ID NO: 1214)								
IALPhs	P 528	(SEQ ID NO: 1212)								
Consensus	X	(SEQ ID NO: 1215)								

FIG. 10
ALP-TNALP Consensus Sequences Excluding Pathogenic Mutations

XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	PXXWXXXAXX	XLXXAXXLQX	XXXXXXXXAKNXI	60
XFLGDGMGVX	TVTAXRILKG	QXXXXXXXXGXEX	XLXMDXFFPX	ALSKTYXXXX	XVPDSXXTAT	120
AYLCGVKXNX	XTXGXSAAAX	XXXCNTTXGN	EVTXXXXXAK	XXGKSVGXVT	TTRVXHAXPX	180
XXYAHXXXXRX	WYSDXXXXPXX	AXXXGCXDIA	XQLXXNXXDI	XVIXGGGRKY	MXXXXXXXDXE	240
YXXDXXXXXGX	RLDGXXLXXX	WXXXXXXXXXX	XXXXWNRTXL	XXXXXXXXXXVX	XLXGLFXPGD	300
MYEXXRXXX	XDPSLXEMXX	XAXXXLXXXX	XGFXLXVEGG	RIDHGHXXX	AXXALXEXXX	360
XDXAIXXAGX	XTSXXDTLXX	VTADHSHVFX	FGYXXRXXS	IFGLAPXXXX	XDXXXXTXXL	420
YGNPGYXXX	XGXRXXVXXX	XXXXXXXXYXXQ	XAVPLXXETH	XGEDVAVFXX	GPXAHLXHGV	480
XEQXXXXHVM	AXAXCXXXXX	XXXXXXXXAXX	XXXXXXXXXXXX	XXXXLXXXXX	XXLXXXXXXX	540
					X	541

(SEQ ID NO: 1218)

FIG. 11
TNALP Consensus Sequences Excluding Pathogenic Mutations

MIXPFLXLAI	GTCXXXSXVP	EKEXDPXYWR	XQAQXTLKXA	LXLQXLNTNV	AKNXIMFLGD	60
GMGVSTVTAX	RILKGQLHHX	XGEETXLEMD	KFPXVALSKT	YNTNAQVPDS	AGTATAYLCG	120
VKANEGTVGV	SAATXRXXCN	TTQNEVTSI	LRWAKDXGKS	VGIVTTTRVN	HATPSAXYAH	180
SADRDWYSDN	EMPPEALSQG	CKDIAYQLMX	NXXDIXVIMG	GGRKYMXPKN	XTDVEYEXDE	240
KXXGXRLDGL	XLXXXWKXFK	PXXKHSXXXW	NRTXLLXLDP	XXVDYLLGLF	XPGDMQYELN	300
RNXXTDPSLS	EMVXXAXXIL	XKXXXGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDXAIG	360
XAGXXTSXXD	TLTXVTADHS	HVFTFGGYTP	RGNSIFGLAP	MXSDTDKKPF	TXILYGNPGP	420
YKVVXGEREN	VSMVDYAHNN	YQAQSAVPLR	HETHGGEDVA	VFXKGPM AHL	LHGVXEQNYX	480
PHVMAYAXCI	GANXXHCAXA	XSXXXXXXGX	LXLXAXXXX	XXLF		524

(SEQ ID NO: 1219)

FIG. 12
Multiple Sequence Alignment of Natriuretic Peptides

Human ANP	-----SLRRSS	CFGGRMDRIGAQSGGLGC	NSFRY-----	(SEQ ID NO: 1)
Human urodilatin	TAPRSLRRSS	CFGGRMDRIGAQSGGLGC	NSFRY-----	(SEQ ID NO: 2)
Human BNP	-SPKMVQSGG	CFGRKMDRISSSSGLGCKVLRH-----		(SEQ ID NO: 3)
Human CNP22	-----GLSKG	CFGLKLDRI GSM SGLGC	-----	(SEQ ID NO: 4)
DNP	-----EVKYDPP	CFGHKIDRINHVS N LGC	PSLRDPRPNAPSTSA	(SEQ ID NO: 5)
	*** ::***. *.***			
CONSENSUS SEQUENCE		CFGXXXDRIXXXSXLGC		(SEQ ID NO: 6)

FIG. 13

Sequences of Human CNP53, CNP22, and CNP (ring only)

Human CNP53	DLRVDTKSRAAWARLLQEHFNARKYKGANKKGLSKG	CFGLKLDRI GS MSGLGC	(SEQ ID NO: 11)
Human CNP22	-----GLSKG	CFGLKLDRI GS MSGLGC	(SEQ ID NO: 4)
Human CNP (ring only)	-----	CFGLKLDRI GS MSGLGC	(SEQ ID NO: 12)

FIG. 14

Multiple Sequence Alignment of C-Type Natriuretic Peptides from Various Species

Human	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 4)
Bovine	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 13)
Sheep	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 14)
Mouse	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 15)
Pig	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 16)
Micrurus fulvius fulvius	GLAKEALGDG CFGLKLDRI GTSS GLGC	(SEQ ID NO: 17)
Taeniopygia guttata	-----G CFGLKLDRI GTFF SLGC	(SEQ ID NO: 18)
Chicken	-----GLSR SCF GVKLDRI GSM SLGC	(SEQ ID NO: 19)
Rana catesbeiana	-----SRG CF GVKLDRI GA FS GLGC	(SEQ ID NO: 20)
Eel	-----GWN RCF GLKLDRI GS LS GLGC	(SEQ ID NO: 21)
Trout	-----GWN RCF GLKLDRI GSM SLGC	(SEQ ID NO: 22)
Ornithorhynchus anatinus	-----GLSKG CFGLKLDRI GST SLGC	(SEQ ID NO: 23)
Trimeresurus flavoviridis	-----K GCF GHKLDRI GS TS GLGC	(SEQ ID NO: 24)
Polypterus endlicheri	-----SKG CF GLKLDRI GS IS GLGC	(SEQ ID NO: 25)
Xenopus laevis	-----LSKG CFGLKLDRI GV VS GLGC	(SEQ ID NO: 26)
Oryzias latipes	-----G CF GMKMDRI GS IS GLGC	(SEQ ID NO: 27)
Tetraodon nigroviridis	-----G CF GMKIDRI GS IS GLGC	(SEQ ID NO: 28)
Pseudechis australis	-----SKIGD GCF GLPLDHI GS VS GLGC	(SEQ ID NO: 29)
	*** :*:*** *****	
CONSENSUS SEQUENCE	XXXXXXXXXX CFGXXDXIGXXSGLGC	(SEQ ID NO: 30)

FIG. 15A

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

```

sp|Q8AYR5|ANFC2_ORYLA      ---MAVCSSSS-----LILLTVFLSVAVETRP--SSDRDE----- 30
sp|Q805D5|ANFC2_TAKRU      ---MAASSSSF-----VPLVLLFLAIPVEPRP--SMTRDE----- 30
sp|Q76KW6|ANFC_ACITR       ---MSISSSSSSSSSSSSCLLLISLMLLAASCQGRPDLQHRNH----- 40
sp|Q61839|ANFC_MOUSE      ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
tr|Q544K5|Q544K5_MOUSE    ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
tr|Q8VHG9|Q8VHG9_NOTAL    ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
sp|P55207|ANFC_RAT         ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
sp|P55206|ANFC_BOVIN       ---MHLSQLL-----ACALLLALLSLRPSEAKPGAP----- 28
sp|P56283|ANFC_SHEEP      ---MHLSQLL-----ACALLSLLSLRPSEAKPGAP----- 28
sp|P18104|ANFC_PIG        ---MHLSQLL-----ACALLLTLLSLRPSEAKPGAP----- 28
sp|P23582|ANFC_HUMAN       ---MHLSQLL-----ACALLLTLLSLRPSEAKPGAP----- 28
sp|P84715|ANF39_ORNAN     ---MHLSHLL-----AWALLLTLLSLR--AEAKPPSPQ----- 28
tr|Q9QZ96|Q9QZ96_CAVPO    -----
sp|Q80017|ANFC4_ORYLA     ---MNL SYLV-----ACGLLVTFLSDK--MDAQPLTPAQ----- 29
sp|Q805D3|ANFC4_TAKRU     ---MNL SYLV-----ACGLMITLLSVR--MGAKPLSQAQ----- 29
tr|C1BXI5|C1BXI5_ESOLU    ---MNL SYLV-----ACGLMITLLSVR--SGAKPLTAAQ----- 29
tr|D2KXA5|D2KXA5_ANGJA    ---MNVSQLM-----VCGLLMALFSFS--TEAKSLIPAQ----- 29
tr|Q1XGY7|Q1XGY7_9ACTI    ---MNL SHLV-----ACGLLVALLTVT--MEAKPLTQSQ----- 29
sp|P40756|ANFD_RANCA      ---MHFCHIV-----CWGLVLAVLYLR--TEAKPVAQAH----- 29
sp|P0C7P5|BNP_TRIFL       ---MFVSRLA-----ASGLLLLALLLALSLDGKPVHQS KPGR----- 33
sp|P0C7P6|BNP_TRIGA       ---MFVSRLA-----ASGLLLLALLLALSLDGKPVQE--KPGR----- 32
sp|Q6LEM5|BNP1_BOTJA      ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQS----- 32
sp|Q9PW56|BNP2_BOTJA      ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQGG----- 33
sp|P68515|BNP_BOTIN       ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQGG----- 33
sp|Q90Y12|BNP_CRODU       ---MFVSRLA-----ASGLLLLALLLAVSLDGKPLQQWS----- 30
sp|Q2PE51|BNP_CRODO       ---MFVSRLA-----ASGLLLLALLLAVSLDGKPLQQWS----- 30
sp|B0VXV8|BNP_SISCA       ---MFVSRLA-----ASGLLLLALLLAVSLDGKPVQQWS----- 30
sp|Q27J49|BNP_LACMU       ---MFVSRLA-----ASGLLLLALLLAVSLDGKPVQQWSH----- 31
sp|P01021|BNP_AKGHA       ---MFVSRLA-----ASGLLLLALMALSLDGKPVQQWSQGRPPGPPI 39
sp|Q09GK2|VNP_PHIOL       ---MVASRLA-----AGGLLLLALLLALALDGKPAPP--QP----- 30
tr|D1MZV3|D1MZV3_RHATT    ---MFASRLA-----ALG LLLLALV---LDGKPAPPPQP----- 28
tr|Q7T1M4|Q7T1M4_BOTJR    ---HEKPSRSG-----AKSAAVGA KLAASSD SAADECSSGRK----- 34
tr|Q402A2|Q402A2_PETMA    -----
tr|Q402A3|Q402A3_LAMJA    ---MKLQLLMMV-----VVVGSWTF LG---VGAKPLT SYELYD----- 32
tr|Q402A1|Q402A1_9PETR    ---MRRQVLVMV-----VMVVVMVMSGKSVTAKPVASYELLD----- 35
sp|P21805|ANFC_CHICK      -----
tr|A9CDT6|A9CDT6_CHICK    ---MKLLFC-----PGFFLLLIVSQKQAMAKPIS----- 26
sp|P20968|ANFC_RANCA      ---MSYKRGTC-----LGFIMLLMVSHHHTKGKPLS----- 28
sp|P55208|ANFC_TRISC      ---MSGQTSFY-----CGLLLVLLLIQAQ---ARPRS----- 25
sp|P23259|ANFC_SCYCA      -----RPRS----- 4
sp|P41319|ANFC_SQUAC      ---MSGHTSFY-----CGLLLLLLLIQVQ---ARPR----- 25
tr|Q2MH72|Q2MH72_9CHON    ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH73|Q2MH73_9CHON    ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH71|Q2MH71_9CHON    ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH74|Q2MH74_DASAK    ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2PF87|Q2PF87_CALMI    ---MNAHVSFP-----CGLMLLLLIIQVQVQ---ARPTG----- 28
sp|Q80018|ANFC3_ORYLA     ---MSLRAF-----MLCVCLLLQSVG---ARPAS----- 23
tr|Q4ADV1|Q4ADV1_ORYLA    ---MSLRAF-----MLCVCLLLQSVG---ARPAS----- 23
sp|Q805D4|ANFC3_TAKRU     ---MSLNLPGY-----ALFFILLVASSG---AKPAP----- 25
tr|C0H7B0|C0H7B0_SALSA    ---MKMISNIQFF-----CLTALVLLNLVG---ANPMS----- 27
tr|C1BWD1|C1BWD1_ESOLU    ---MISNIQFC-----CLSVLVLLNLVG---AKPVS----- 25
tr|D2KXA3|D2KXA3_ANGJA    ---MISNITIY-----CISLFLNLVG---GKPVS----- 25
tr|B3DJJ2|B3DJJ2_DANRE    ---MIANISVF-----CVSSLLLLNLVG---AKPVS----- 25
tr|Q1XGY8|Q1XGY8_9ACTI    ---MVSRLTVY-----CALFIIVLSQVS---AKPVS----- 25
sp|Q8AXR2|ANFC2_ONCMY     ---ML--YPA-----LLCAALLLIAPLGHTEGRTL YSPD----- 30
sp|Q8AXR3|ANFC1_ONCMY     ---ML--YPA-----LLCAALLLIAPLGHTEGRTL HPSD----- 30
tr|C1BKS8|C1BKS8_OSMO     ---ML--CPV-----LLCATLVLLPPELSEGRALHPSPE----- 30
tr|Q805E7|Q805E7_OREMO     ---ML--CPV-----LLCAALLLLTPLEITEARALHPSPD----- 30
tr|C3KH23|C3KH23_ANOFI    ---ML--CPV-----LLCATLLLLTPLEITEARALHPPD----- 30
sp|Q8AYR6|ANFC1_ORYLA     ---ML--CPV-----LLCATLLLLTPFEVTEARALHPSAD----- 30
sp|Q805D6|ANFC1_TAKRU     ---ML--CPA-----LLCAALLLLTPVEITDARALQQPSD----- 30
sp|P18145|ANFC_ANGJA      ---MM--CKA-----LVFAVLLLAVPLERADSRALRTPVD----- 30
tr|Q1XGY9|Q1XGY9_9ACTI    ---MMGSCSAPLLTGHRILCLFLLMASSLSPIHSRAFRSPP----- 38
tr|A9CDT5|A9CDT5_CHICK    MLGLPA-----WPCSLFLLLVLLSASVQAMSSSGQR----- 31

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FIG. 15B**Multiple Alignment of C-Type Natriuretic Peptides from Various Species**

```

sp|Q8AYR5|ANFC2_ORYLA -----
sp|Q805D5|ANFC2_TAKRU -----
sp|Q76KW6|ANFC_ACITR -----
sp|Q61839|ANFC_MOUSE -----
tr|Q544K5|Q544K5_MOUSE -----
tr|Q8VHG9|Q8VHG9_NOTAL -----
sp|P55207|ANFC_RAT -----
sp|P55206|ANFC_BOVIN -----
sp|P56283|ANFC_SHEEP -----
sp|P18104|ANFC_PIG -----
sp|P23582|ANFC_HUMAN -----
sp|P84715|ANF39_ORNAN -----
tr|Q9QZ96|Q9QZ96_CAVPO -----
sp|Q80017|ANFC4_ORYLA -----
sp|Q805D3|ANFC4_TAKRU -----
tr|C1BXI5|C1BXI5_ESOLU -----
tr|D2KXA5|D2KXA5_ANGJA -----
tr|Q1XGY7|Q1XGY7_9ACTI -----
sp|P40756|ANFD_RANCA -----
sp|P0C7P5|BNP_TRIFL -----SPPIS----- 38
sp|P0C7P6|BNP_TRIGA -----SPPISPLLVP-----PPPPPHWPPP- 53
sp|Q6LEM5|BNP1_BOTJA -----WP--GNIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 69
sp|Q9PW56|BNP2_BOTJA -----WPRPGPEIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 72
sp|P68515|BNP_BOTIN -----WPRPGPEIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 72
sp|Q90Y12|BNP_CRODU -----QRWP--- 34
sp|Q2PE51|BNP_CRODO -----QRWP--- 34
sp|B0VXV8|BNP_SISCA -----QNWPG-- 35
sp|Q27J49|BNP_LACMU -----KGWPPERQIPPLVVQQWSQKPWP-PGHHIPPVVQEWPP-- 69
sp|P01021|BNP_AGKHA PRLVVQQWSQGLPPGPPIPRLVVQQWSQG-LP-PGPPIPPLVVQQWSQGL 87
sp|Q09GK2|VNP_PHIOL -----
tr|D1MZV3|D1MZV3_RHATT -----
tr|Q7T1M4|Q7T1M4_BOTJR -----GEPPG- 39
tr|Q402A2|Q402A2_PETMA -----
tr|Q402A3|Q402A3_LAMJA -----
tr|Q402A1|Q402A1_9PETR -----
sp|P21805|ANFC_CHICK -----
tr|A9CDT6|A9CDT6_CHICK -----
sp|P20968|ANFC_RANCA -----
sp|P55208|ANFC_TRISC -----
sp|P23259|ANFC_SCYCA -----
sp|P41319|ANFC_SQUAC -----
tr|Q2MH72|Q2MH72_9CHON -----
tr|Q2MH73|Q2MH73_9CHON -----
tr|Q2MH71|Q2MH71_9CHON -----
tr|Q2MH74|Q2MH74_DASAK -----
tr|Q2PF87|Q2PF87_CALMI -----
sp|Q80018|ANFC3_ORYLA -----
tr|Q4ADV1|Q4ADV1_ORYLA -----
sp|Q805D4|ANFC3_TAKRU -----
tr|C0H7B0|C0H7B0_SALSA -----
tr|C1BWD1|C1BWD1_ESOLU -----
tr|D2KXA3|D2KXA3_ANGJA -----
tr|B3DJJ2|B3DJJ2_DANRE -----
tr|Q1XGY8|Q1XGY8_9ACTI -----
sp|Q8AXR2|ANFC2_ONCMY -----
sp|Q8AXR3|ANFC1_ONCMY -----
tr|C1BKS8|C1BKS8_OSMMO -----
tr|Q805E7|Q805E7_OREMO -----
tr|C3KH23|C3KH23_ANOFI -----
sp|Q8AYR6|ANFC1_ORYLA -----
sp|Q805D6|ANFC1_TAKRU -----
sp|P18145|ANFC_ANGJA -----
tr|Q1XGY9|Q1XGY9_9ACTI -----
tr|A9CDT5|A9CDT5_CHICK -----

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FIG. 15C**Multiple Alignment of C-Type Natriuretic Peptides from Various Species**

```

sp|Q8AYR5|ANFC2_ORYLA -----
sp|Q805D5|ANFC2_TAKRU -----
sp|Q76KW6|ANFC_ACITR -----
sp|Q61839|ANFC_MOUSE -----
tr|Q544K5|Q544K5_MOUSE -----
tr|Q8VHG9|Q8VHG9_NOTAL -----
sp|P55207|ANFC_RAT -----
sp|P55206|ANFC_BOVIN -----
sp|P56283|ANFC_SHEEP -----
sp|P18104|ANFC_PIG -----
sp|P23582|ANFC_HUMAN -----
sp|P84715|ANF39_ORNAN -----
tr|Q9QZ96|Q9QZ96_CAVPO -----
sp|Q800I7|ANFC4_ORYLA -----
sp|Q805D3|ANFC4_TAKRU -----
tr|C1BXI5|C1BXI5_ESOLU -----
tr|D2KXA5|D2KXA5_ANGJA -----
tr|Q1XGY7|Q1XGY7_9ACTI -----
sp|P40756|ANFD_RANCA -----
sp|P0C7P5|BNP_TRIFL -----PLSAQQWMPEGRPPHP--IPPLSVQQWSQGRP----- 68
sp|P0C7P6|BNP_TRIGA ---HHIPPLSVQKFPFGWKPTHPHHIPPLEVQQWSQGGP----- 89
sp|Q6LEM5|BNP1_BOTJA WPHPQIPPLTVQQWAQ-GRAPGPP-IPPLTVQQWAQGRAPHPPIPPAPLQ 117
sp|Q9PW56|BNP2_BOTJA WPHPQIPPLTVQQWAQWGRPPGPP-IPPLTVQQWAQARPPHPPIPPAPLQ 121
sp|P68515|BNP_BOTIN WPHPQIPPLTVQQWAQLGPPPRPQ-IPPLEVQQWAQGRAPHPPIPPAPLQ 121
sp|Q90Y12|BNP_CRODU -----HLE-IPPLVVQNWK----- 47
sp|Q2PE51|BNP_CRODO -----HLE-IPPLVVQNWK----- 47
sp|B0VXV8|BNP_SISCA ---PKVPPLVVQQWSQN--WPHPQ-IPPLVVQNWK----- 64
sp|Q27J49|BNP_LACMU --GHHIPPLVVQQWSQKKWPPGHH-IPPLVVQKWDP----- 102
sp|P01021|BNP_AGKHA PPRPKIPPLVVQQWSQG-LPPRPK-IPPLVVQKWDP----- 121
sp|Q09GK2|VNP_PHIOL -----
tr|D1MZV3|D1MZV3_RHATT -----
tr|Q7T1M4|Q7T1M4_BOTJR ---PIIPPLTVQQWAQAR-PPHPP-IPPAPLQKWAPVQK----- 73
tr|Q402A2|Q402A2_PETMA -----
tr|Q402A3|Q402A3_LAMJA -----
tr|Q402A1|Q402A1_9PETR -----
sp|P21805|ANFC_CHICK -----
tr|A9CDT6|A9CDT6_CHICK -----
sp|P20968|ANFC_RANCA -----
sp|P55208|ANFC_TRISC -----
sp|P23259|ANFC_SCYCA -----
sp|P41319|ANFC_SQUAC -----
tr|Q2MH72|Q2MH72_9CHON -----
tr|Q2MH73|Q2MH73_9CHON -----
tr|Q2MH71|Q2MH71_9CHON -----
tr|Q2MH74|Q2MH74_DASAK -----
tr|Q2PF87|Q2PF87_CALMI -----
sp|Q800I8|ANFC3_ORYLA -----
tr|Q4ADV1|Q4ADV1_ORYLA -----
sp|Q805D4|ANFC3_TAKRU -----
tr|C0H7B0|C0H7B0_SALSA -----
tr|C1BWD1|C1BWD1_ESOLU -----
tr|D2KXA3|D2KXA3_ANGJA -----
tr|B3DJJ2|B3DJJ2_DANRE -----
tr|Q1XGY8|Q1XGY8_9ACTI -----
sp|Q8AXR2|ANFC2_ONCMY -----
sp|Q8AXR3|ANFC1_ONCMY -----
tr|C1BKS8|C1BKS8_OSMMO -----
tr|Q805E7|Q805E7_OREMO -----
tr|C3KH23|C3KH23_ANOFI -----
sp|Q8AYR6|ANFC1_ORYLA -----
sp|Q805D6|ANFC1_TAKRU -----
sp|P18145|ANFC_ANGJA -----
tr|Q1XGY9|Q1XGY9_9ACTI -----
tr|A9CDT5|A9CDT5_CHICK -----

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FIG. 15D

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

sp Q8AYR5 ANFC2_ORYLA	-----EQVLKSLFGPHLTSL-----IL	47
sp Q805D5 ANFC2_TAKRU	-----AQVLRALFGARLSSI-----IS	47
sp Q76KW6 ANFC_ACITR	-----KSQLAGLFGAEVAAL-----LE	57
sp Q61839 ANFC_MOUSE	-----PKVPRTPPGEEELADS-----QAAG	47
tr Q544K5 Q544K5_MOUSE	-----PKVPRTPPGEEELADS-----QAAG	47
tr Q8VHG9 Q8VHG9_NOTAL	-----PKVPRTPPGEEELADS-----QAAG	47
sp P55207 ANFC_RAT	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P55206 ANFC_BOVIN	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P56283 ANFC_SHEEP	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P18104 ANFC_PIG	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P23582 ANFC_HUMAN	-----PKVPRTPPAEEELAEP-----QAAG	47
sp P84715 ANF39_ORNAN	-----PQVPRSP-GDEASEA-----VAAN	46
tr Q9QZ96 Q9QZ96_CAVPO	-----	
sp Q80017 ANFC4_ORYLA	-----QKSLRSLLGEEELAEF-----LESG	48
sp Q805D3 ANFC4_TAKRU	-----QKSFRSLLGEEELAEF-----LESE	48
tr C1BXI5 C1BXI5_ESOLU	-----QKSLRNLLGEEELSEF-----LASG	48
tr D2KXA5 D2KXA5_ANGJA	-----EKSLRNLLGEEELSEY-----LASG	48
tr Q1XGY7 Q1XGY7_ACTI	-----QKSLRNLLGEEELSAI-----LTSD	48
sp P40756 ANFD_RANCA	-----QKSLRALLGEEELAEY-----LVSG	48
sp P0C7P5 BNP_TRIFL	---RSEVPPVVVQPHESPAGGTTAFREELSPG-----PEAASG	103
sp P0C7P6 BNP_TRIGA	---RSEL---VQPHESPAGGTTAFREELSLG-----PEAASG	120
sp Q6LEM5 BNP1_BOTJA	KWAPLQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	155
sp Q9PW56 BNP2_BOTJA	KWAPVQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	159
sp P68515 BNP_BOTIN	KWAPVQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	159
sp Q90Y12 BNP_CRODU	-----SPTQLQARESPAGGTTALREELSLG-----PEAALD	78
sp Q2PE51 BNP_CRODO	-----SPTQLQARESPAGGTTALREELSLG-----PEAALD	78
sp B0VXV8 BNP_SISCA	-----SPTQLQPRESPAGGTTALREELSLG-----PDAALD	95
sp Q27J49 BNP_LACMU	---PPI-SPPLLKPHESPAGGTTALREELSLG-----PEAALD	136
sp P01021 BNP_AGKHA	---PPVSPPLLQPHESPAGGTTALREELSLG-----PEAASG	156
sp Q09GK2 VNP_PHIOL	-----LRKAPAGGTTAWRRELTEQ-----PEGASR	55
tr D1MZV3 D1MZV3_RHATT	-----LRKAPAGGTTALQRQLTEQQQQQQ-----QAEQSSG	59
tr Q7T1M4 Q7T1M4_BOTJR	-WAPVQKWAPLLQPHESPAGGTTALREELSLG-----PEAASG	110
tr Q402A2 Q402A2_PETMA	-----SGSEPWEGG-FLPRVSSSSSSSSG-----EVEPLAE	30
tr Q402A3 Q402A3_LAMJA	-----DAGSEPWEGG-FLPRISSSSSSSS-----AERLAD	60
tr Q402A1 Q402A1_9PETR	-----DTNSEPWEGGSLPSLPSQEGED-----SHPLS-	63
sp P21805 ANFC_CHICK	-----	
tr A9CDT6 A9CDT6_CHICK	-----SLQSLSMILLDEE-----L	39
sp P20968 ANFC_RANCA	-----SLQNLRLLEDN-----F	41
sp P55208 ANFC_TRISC	-----DDSLQTLRLLEDE-----Y	40
sp P23259 ANFC_SCYCA	-----DDSLQTLRLLEDE-----Y	19
sp P41319 ANFC_SQUAC	-----DDSLQVLSRLLEDE-----Y	40
tr Q2MH72 Q2MH72_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH73 Q2MH73_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH71 Q2MH71_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH74 Q2MH74_DASAK	-----DDSLQALTRLLEDE-----Y	40
tr Q2PF87 Q2PF87_CALMI	-----VDSLQILSRLEDE-----Y	43
sp Q80018 ANFC3_ORYLA	-----ELQNLERLL-----	32
tr Q4ADV1 Q4ADV1_ORYLA	-----ELQNLERLL-----	32
sp Q805D4 ANFC3_TAKRU	-----DLQILEPPLSSLEEQQEEMQEEVQEKVQEQQEEVQ	59
tr C0H7B0 C0H7B0_SALSA	-----NLQSLKQLLEEE-----SH	41
tr C1BWD1 C1BWD1_ESOLU	-----NLQSLKEFLEE-----SN	38
tr D2KXA3 D2KXA3_ANGJA	-----SLQSLKELLEEE-----SN	39
tr B3DJJ2 B3DJJ2_DANRE	-----SLQSLKQLLEDE-----VN	39
tr Q1XGY8 Q1XGY8_ACTI	-----SLQSFAQLLEDE-----SN	39
sp Q8AXR2 ANFC2_ONCMY	-----AIQFVEQFLDR-----YN	43
sp Q8AXR3 ANFC1_ONCMY	-----AIQFVEQFLDR-----YN	43
tr C1BKS8 C1BKS8_OSMMO	-----GLQFVEQFLER-----CT	43
tr Q805E7 Q805E7_OREMO	-----AVQFVEQFLER-----YN	43
tr C3KH23 C3KH23_ANOFI	-----AVQFMEQFLER-----YN	43
sp Q8AYR6 ANFC1_ORYLA	-----AVQFVEQFLDR-----YN	43
sp Q805D6 ANFC1_TAKRU	-----AAQFMEQFLER-----YN	43
sp P18145 ANFC_ANGJA	-----AIQFVEQFLEH-----YN	43
tr Q1XGY9 Q1XGY9_ACTI	-----LQFLSTLLEKE-----YG	51
tr A9CDT5 A9CDT5_CHICK	-----LQVLLSLLPS-----DS	44

FIG. 15E

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

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sp|Q8AYR5|ANFC2_ORYLA      APPTSND--TEGSSGSPEPP-----TPSEAPVLIH-- 76
sp|Q805D5|ANFC2_TAKRU      TPVNTDDI--AELLRRPGPPR-----SFGASPGALRGLTR-- 81
sp|Q76KW6|ANFC_ACITR       DAGAADGSSGEEAALSQRAPPS-----IRALHPRSGRLGLRDD 95
sp|Q61839|ANFC_MOUSE      GNQKKGDKTPGSGGANLKGDRS-----RLLRDRLR 76
tr|Q544K5|Q544K5_MOUSE    GNQKKGDKTPGSGGANLKGDRS-----RLLRDRLR 76
tr|Q8VHG9|Q8VHG9_NOTAL    GNQKKGDKTPGGGGANLKGDRSRLKGDTPGGGGANLKGDRSRLLRDLR 97
sp|P55207|ANFC_RAT        GNQKKGDKTPGGGGANLKGDRS-----RLLRDRLR 76
sp|P55206|ANFC_BOVIN      GGQKKGDKTPGGGGANLKDDRS-----RLLRDRLR 76
sp|P56283|ANFC_SHEEP      GGQKKGDKTPGGGGANLKDDRS-----RLLRDRLR 76
sp|P18104|ANFC_PIG        GGQKKGDKTPGGGGANLKGDRS-----RLLRDRLR 76
sp|P23582|ANFC_HUMAN      GGQKKGDKAPGGGGANLKGDRS-----RLLRDRLR 76
sp|P84715|ANF39_ORNAN     GGKKKGDKKP-----KGRDP-----RLLRELR 68
tr|Q9QZ96|Q9QZ96_CAVPO    -----
sp|Q80017|ANFC4_ORYLA     ENENRLDDVRSRM-----RLLRDRLR 68
sp|Q805D3|ANFC4_TAKRU     EKERRLDAVRSRL-----RLLRDRLR 68
tr|C1BXI5|C1BXI5_ESOLU    ERERRLDTVRSRV-----RLLRDRLR 68
tr|D2KXA5|D2KXA5_ANGJA    EREERNLESARS-----RLLRDRLR 66
tr|Q1XGY7|Q1XGY7_9ACTI    EQESGSENLRSA-----RLLRDRLR 68
sp|P40756|ANFD_RANCA      ERGERSIDPKTRA-----RLLRDIR 68
sp|P0C7P5|BNP_TRIFL      -----PAAPHRLPKSKG-----ASATS-AASRPMRDRLR 130
sp|P0C7P6|BNP_TRIGA      -----PAAPQRLPKRKG-----ASATS-AASRSMRDRLR 147
sp|Q6LEM5|BNP1_BOTJA      VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAAT-----RPMRDRLR 193
sp|Q9PW56|BNP2_BOTJA      VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAATS-AASRPMRDRLR 201
sp|P68515|BNP_BOTIN      VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAATS-AASRPMRDRLR 201
sp|Q90Y12|BNP_CRODU      TPPAGPDGGRSGSKAAAAAPQRLSKSKG-----ASATS-AASR---DLR 118
sp|Q2PE51|BNP_CRODO      TPPAGPDGGRSGSKAAAAAPQRLSKSKG-----ASATS-AASR---DLR 118
sp|B0VXV8|BNP_SISCA      TPPAGPDVGPRGSK-AAAAPQRLSKSKG-----ASATS-TASRPMRDRLR 137
sp|Q27J49|BNP_LACMU      TPPAGPDVGPRGSK-APAAPHRLPKSKG-----ASATS-AASRPMRDRLR 178
sp|P01021|BNP_AGKHA      PAAAGADGGRSGSK-APAALHRLSKSKG-----ASATSASASRPMRDRLR 199
sp|Q09GK2|VNP_PHIOL      PAAGGGGGGGRSGSKAANAAPTAPKSKG-----AAAAAAAARLMDRLR 100
tr|D1MZV3|D1MZV3_RHATT    PAAGGGGG--RSGSKTANAAPTAPKSKG-----AAASAASRLLRDLR 99
tr|Q7T1M4|Q7T1M4_BOTJR    VPSAGAEGRAQRLEGARCTPSAVEEQRGG-----GDLGGVAADAGLAPRR 155
tr|Q402A2|Q402A2_PETMA    VTATGGVSGGVSGVLGGTPWVGPRGHQ-----RPSRGLA 65
tr|Q402A3|Q402A3_LAMJA    ATVTR-HGGGGGGGGDDGTSWELPQGPPG-----PPRSSRGLA 97
tr|Q402A1|Q402A1_9PETR    -----AEGG-----PWERGSGPQ-----RSSRGIG 83
tr|P21805|ANFC_CHICK      -----
tr|A9CDT6|A9CDT6_CHICK    QHPLVSEERDREQDGSIPVGAF-----DQEDAEFQWTRNTRD----- 76
sp|P20968|ANFC_RANCA      ERSFGSDEADQQL---VPTDSL-----DQLDPELQWNKNRLE----- 75
sp|P55208|ANFC_TRISC      GHYLPSEDLNNEAQEMSPAASLPEFNADQSDLELPWDRESRE----- 82
sp|P23259|ANFC_SCYCA      GHYLPSEDLNNEAEEMSPAASLPELNADQSDLELPWERESRE----- 61
sp|P41319|ANFC_SQUAC      GHFN-SEELNNEAQEISPAASLPDLNTDQSDLELPWDRESRE----- 81
tr|Q2MH72|Q2MH72_9CHON    GQYFTTEDLNNEAPEIPPAASLPDLNTDQSDLDLSWDRESRE----- 82
tr|Q2MH73|Q2MH73_9CHON    GQYFTTEDLNNEAPEIPPAASLPDLNTDQSDLDLSWDRESRE----- 82
tr|Q2MH71|Q2MH71_9CHON    GQYFTSEDLNNEAPEIPPAASLPDLNTDQPDFDLSDWDRESRE----- 82
tr|Q2MH74|Q2MH74_DASAK    GQYFTSEDLNNEAPEMSPAASLPDLNTEQSETDLPWDRESRE----- 82
tr|Q2PF87|Q2PF87_CALMI    GPYLSSEDSMEAEASRAGTLRLDNLQADMDLLWDRDARD----- 85
sp|Q80018|ANFC3_ORYLA     ---QDQLSSTEHPPEE---DRLD---RTREEPQLGG----- 58
tr|Q4ADV1|Q4ADV1_ORYLA    ---QDQLSSTEHPPEE---DRLD---RTREEPQLGG----- 58
sp|Q805D4|ANFC3_TAKRU     EKVQEQQEEVQEQQEEVQEQQE-----EQQEEVQERGRGTGDVLLRAQLD 104
tr|C0H7B0|C0H7B0_SALSA    VPHYASDEMVGDKDLNTEN-----IAEEVPPWDSedar----- 75
tr|C1BWD1|C1BWD1_ESOLU    VPYYGSESEVDKDLNTEKEA-----FTGEVVPWLTEDR----- 74
tr|D2KXA3|D2KXA3_ANGJA    APYLDSEEAQVQKEMNAENAA-----FTKASLHSDWPNSR----- 75
tr|B3DJJ2|B3DJJ2_DANRE    KPFEESQESVMEQKDATAEKSA-----LDERAEQLWESDAR----- 75
tr|Q1XGY8|Q1XGY8_9ACTI    HPYVSDDDTRGGLDVSAEIAT-----DDSEADIPWNHNRDL----- 77
sp|Q8AXR2|ANFC2_ONCMY     DLT--LDDLLENLVSSQPEEPSS-----AFTSGVKIAEYPKW 77
sp|Q8AXR3|ANFC1_ONCMY     DLT--LDDLLENLVSSQPEEPSS-----AFTSGVKVAEYPKW 77
tr|C1BKS8|C1BKS8_OSMO     DLLN-LDDLLENAGSNQPEEPS-----DYANGVKVAEYPKW 77
tr|Q805E7|Q805E7_OREMO    DLLT-LDDLLENMLNSQAEQES-----TLSSGSKAVEYPKW 77
tr|C3KH23|C3KH23_ANOFI    DLLT-LDDLLENLINSQPEEQS-----TFSSGVKAAEYPKW 77
sp|Q8AYR6|ANFC1_ORYLA     DLLT-LDDLLENLNTQPEEQS-----TLSSGVKTAIEYPKW 77
sp|Q805D6|ANFC1_TAKRU    DLLT-LDDLLENMLNSHPEDQS-----NLSS-SKADEYPKW 76
sp|P18145|ANFC_ANGJA      DLLN-IDDLLENQTGDQLESPQ-----PLSSGLKVAEYPKW 77
tr|Q1XGY9|Q1XGY9_9ACTI    NLQSGPVNIHNVSSSEQYEDPQ-----PWADVSSVSKEQI 86
tr|A9CDT5|A9CDT5_CHICK    ESMPAEEDMKEGSSSEPQLLSP-----PLPLPSRAR----- 76

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FIG. 15F

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

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sp|Q8AYR5|ANFC2_ORYLA      -----GDRGTASQILRSFLRQRE-----KTRRWG--RKPMVAG- 107
sp|Q805D5|ANFC2_TAKRU      -----GSEG-GSRFLLDFLQQQS-----KTTRRG--RSSMVGG- 111
sp|Q76KW6|ANFC_ACITR      LEAEPPAENKPRRRLKDFMSSR-----KMFRGR--TKMKQQG- 131
sp|Q61839|ANFC_MOUSE      VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
tr|Q544K5|Q544K5_MOUSE    VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
tr|Q8VHG9|Q8VHG9_NOTAL    VDTKSR---AAWARLLHEHPN-----ARKNKG--GNKKGLS- 128
sp|P55207|ANFC_RAT        VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
sp|P55206|ANFC_BOVIN      VDTKSR---AAWTRLLEHPN-----ARKYKG--GNKKGLS- 107
sp|P56283|ANFC_SHEEP      VDTKSR---AAWTRLLEHPN-----ARKYKG--GNKKGLS- 107
sp|P18104|ANFC_PIG        VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
sp|P23582|ANFC_HUMAN      VDTKSR---AAWARLLQEHNP-----ARKYKG--ANKKGLS- 107
sp|P84715|ANF39_ORNAN     LDTRSRSRGRVWTRLHDHPN-----PRKYKP--ANKKGLS- 102
tr|Q9QZ96|Q9QZ96_CAVPO    -----N-----ARKYKG--GNKKGLS- 14
sp|Q80017|ANFC4_ORYLA     VDTRAR---GMWARLLNDQPA-----SRRHKS--GSKKGGST 100
sp|Q805D3|ANFC4_TAKRU     MDTRAR---GVWARLLNDQPV-----PRRHKT--GIKKGGS- 99
tr|C1BXI5|C1BXI5_ESOLU    MDTRAK---GMWARLLNDQPN-----ARRHKQ--NSKKGTV- 99
tr|D2KXA5|D2KXA5_ANGJA    LNTRAR---GMWSRIMNDQPA-----SRKQKT--GVKKGAST 98
tr|Q1XGY7|Q1XGY7_ACTI     LDIRAK---AAWARLLNDHPN-----PRKSKG--INKKGLS- 99
sp|P40756|ANFD_RANCA      ADTRSR---AAWTRLNEHPN-----SRKIKG--INKKGTS- 99
sp|P0C7P5|BNP_TRIFL      TDGKQERQKWG---RMVQPDHHAAPGGGGGGGGG-ARRMKG--LAKKAMG- 174
sp|P0C7P6|BNP_TRIGA      ADGKQARQKWG---RMVQPDHHAAPGGGGGGGGG-ARRLKG--LAKKAVG- 191
sp|Q6LEM5|BNP1_BOTJA      PDGKQARQNWG---RMAHHDHHAAGGGGGGGGG-ARRLKG--LAKKGAA- 237
sp|Q9PW56|BNP2_BOTJA      PDGKQARQNWG---RMVHHDHHAAGGGGGGGGG-ARRLKG--LAKKGAA- 246
sp|P68515|BNP_BOTIN      PDGKQARQNWG---RMVHHDHHAAGGGGGGGGG-ARRLKG--LAKKGAA- 246
sp|Q90Y12|BNP_CRODU      TDGKQARQNWG---RLVSPDHHSAGGGGGGGGG-ARRLKG--LAKKRAG- 162
sp|Q2PE51|BNP_CRODO      TDGKQARQNWG---RLVSPDHHSAGGGGGGGGG-ARRLKG--LAKKRAG- 162
sp|B0VXV8|BNP_SISCA      TDGKQARQNWG---RMLNPDHHSAPGGGGGGGG-ARRLKG--LAKKRAG- 182
sp|Q27J49|BNP_LACMU      TDGKQARQNWG---RMMNPDHHAAGGGGGGGG-ARRLKG--LAKKRVG- 220
sp|P01021|BNP_AKGHA      TDGKQARQNWA---RMVNPDHHAAGGCCCGGGGG-ARRLKG--LVKKGVA- 244
sp|Q09GK2|VNP_PHIOL      PDSKQARAAGW---RMVHPEHHAGGGGGGGGGG-ARRLKG--LAKKGLG- 145
tr|D1MZV3|D1MZV3_RHATT    PDGKQSRAAWG---RMVHPEHHAGGGGGGGGGG-SRRLKG--LPKKGLG- 142
tr|Q7T1M4|Q7T1M4_BOTJR    QAGAAELGPDGAPRPPRPPRSGRRAAAAAAERGARRLKG--LAKKGAA- 202
tr|Q402A2|Q402A2_PETMA    EGGSQVSG-GVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 99
tr|Q402A3|Q402A3_LAMJA    EGGSQVSG-GVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 131
tr|Q402A1|Q402A1_9PETR    -GGSQVSG-EVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 116
sp|P21805|ANFC_CHICK      -----GLS- 3
tr|A9CDT6|A9CDT6_CHICK    QPASTSTADSDVQRILSDLLGL-----PQRYQN--RSKKGLS- 111
sp|P20968|ANFC_RANCA      QGDSPHVNEMTLQQLLNDPVG-----SRRYRQ--RNKKGYS- 110
sp|P55208|ANFC_TRISC      IGGRPFRQEAVLARLLKDLN-----PLRFRG--RSKKGPS- 117
sp|P23259|ANFC_SCYCA      IGGRPFRQEAVLARLLKDLN-----PLRFRG--RSKKGPS- 96
sp|P41319|ANFC_SQUAC      IGGRSFRQEALLARLLKDLN-----PLRFKG--RSKKGPS- 116
tr|Q2MH72|Q2MH72_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH73|Q2MH73_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH71|Q2MH71_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH74|Q2MH74_DASAK    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2PF87|Q2PF87_CALMI    IGGRSFQHDGLLRLKDLTIS-----PLRFNG--RSKKGPS- 120
sp|Q80018|ANFC3_ORYLA     SSSREAADESALTRLFADLLRT-----SKRSWG--RYKKGGM- 93
tr|Q4ADV1|Q4ADV1_ORYLA    SSSREAADESALTRLFADLLRT-----SKRSWG--RYKKGGM- 93
sp|Q805D4|ANFC3_TAKRU     SSTWALQKDDVLMRLFKDLLRT-----SKRSRS--RYKKGGL- 139
tr|C0H7B0|C0H7B0_SALSA    --NSALTGKEDVIARLLNDIMTT-----PKRSWS--RFKKGGL- 109
tr|C1BWD1|C1BWD1_ESOLU    --SALTGENAVARLLSDIMTT-----PKRSWG--RFKKGGM- 107
tr|D2KXA3|D2KXA3_ANGJA    -DAALSSNENALVRLNDILSS-----SKRSWS--RFKKGGL- 109
tr|B3DJJ2|B3DJJ2_DANRE    -NSALAGKYGMFERLLGDLST-----SKRSWS--RFKKGDL- 109
tr|Q1XGY8|Q1XGY8_ACTI     -QHRQAAHSSRMILKLDILTS-----SGRSWD--REKKSGL- 111
sp|Q8AXR2|ANFC2_ONCMY     ADIP-AQGDSTWLRLKGTLAN-----QKRAVT--DRSRRGWN- 112
sp|Q8AXR3|ANFC1_ONCMY     ADIP-AQGDSTWLRLKGTLAN-----QKRAVM--DRSRRGWN- 112
tr|C1BKS8|C1BKS8_OSMO     ADLPAAQEDSAWLRLKAALAN-----QKRAEP--DRSRRAWN- 113
tr|Q805E7|Q805E7_OREMO    ADAQTQPE-TPWLRLKLGALAN-----QKRAEP--DRSRRGWN- 112
tr|C3KH23|C3KH23_ANOFI    ADAQTQAE-TPWLRLKLGAVAN-----QKRAEP--DRSRRGWN- 112
sp|Q8AYR6|ANFC1_ORYLA     ADLQTQPE-TPWFLRLKGALTN-----QKRAEP--DRSRRGWN- 112
sp|Q805D6|ANFC1_TAKRU     AEAD----TPWLRLRGALAN-----QKRAEP--DRSRRGWN- 107
sp|P18145|ANFC_ANGJA      VDVPSOND-NTWFRLRGALAN-----RKRALP--DRAKRGWN- 112
tr|Q1XGY9|Q1XGY9_ACTI     GDEPPANE-NALYLLLRRAAAN-----RTWISA--DRVKKAWS- 121
tr|A9CDT5|A9CDT5_CHICK    -----AAHPLLWRKALAS-----RKRALSGDWAOKAVP- 104

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FIG. 15G

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

sp Q8AYR5 ANFC2_ORYLA	---GG	CFGMKMDRIGSISGLGC	126 (SEQ ID NO: 31)
sp Q805D5 ANFC2_TAKRU	---RG	CFGMKIDRIGSISGLGC	130 (SEQ ID NO: 32)
sp Q76KW6 ANFC_ACITR	---RG	CFGMKLDRI SMSGLGC	150 (SEQ ID NO: 33)
sp Q61839 ANFC_MOUSE	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 34)
tr Q544K5 Q544K5_MOUSE	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 35)
tr Q8VHG9 Q8VHG9_NOTAL	---KG	CFGLKLDRI SMSGLGC	147 (SEQ ID NO: 36)
sp P55207 ANFC_RAT	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 37)
sp P55206 ANFC_BOVIN	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 38)
sp P56283 ANFC_SHEEP	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 39)
sp P18104 ANFC_PIG	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 40)
sp P23582 ANFC_HUMAN	---KG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 41)
sp P84715 ANF39_ORNAN	---KG	CFGLKLDRI GSTSGLGC	121 (SEQ ID NO: 42)
tr Q9QZ96 Q9QZ96_CAVPO	---KG	CFGLKLDRI SMSGLGC	33 (SEQ ID NO: 43)
sp Q80017 ANFC4_ORYLA	-SRSG	CFGHKMDRIGTISGMGC	121 (SEQ ID NO: 44)
sp Q805D3 ANFC4_TAKRU	-SRSG	CFGHKMDRIGTISGMGC	120 (SEQ ID NO: 45)
tr C1BXI5 C1BXI5_ESOLU	-PRSG	CFGQKLDRI GTLSGMGC	121 (SEQ ID NO: 46)
tr D2KXA5 D2KXA5_ANGJA	PARGG	CFGHKLDRI STL SGMGC	120 (SEQ ID NO: 47)
tr Q1XGY7 Q1XGY7_9ACTI	---KG	CFGLKLDRI SMSGLGC	118 (SEQ ID NO: 48)
sp P40756 ANFD_RANCA	---KG	CFGLKLDRI GAMSGLGC	118 (SEQ ID NO: 49)
sp P0C7P5 BNP_TRIFL	---KG	CFGHKLDRI GSTSGLGC	193 (SEQ ID NO: 50)
sp P0C7P6 BNP_TRIGA	---KG	CFGLPLDRI SMSGMGC	210 (SEQ ID NO: 51)
sp Q6LEM5 BNP1_BOTJA	---KG	CFGLKLDRI GTMSGLGC	256 (SEQ ID NO: 52)
sp Q9PW56 BNP2_BOTJA	---KG	CFGLKVDRI GTMSGLGC	265 (SEQ ID NO: 53)
sp P68515 BNP_BOTIN	---KG	CFGLKLDRI GTMSGLGC	265 (SEQ ID NO: 54)
sp Q90Y12 BNP_CRODU	---NG	CFGLKLDRI SMSGLGC	181 (SEQ ID NO: 55)
sp Q2PE51 BNP_CRODO	---NG	CFGLKLDRI SMSGLGC	181 (SEQ ID NO: 56)
sp B0VXV8 BNP_SISCA	---SG	CFGLKLDRI SMSGLGC	201 (SEQ ID NO: 57)
sp Q27J49 BNP_LACMU	---DG	CFGLKLDRI SMSGLGC	239 (SEQ ID NO: 58)
sp P01021 BNP_AKHA	---KG	CFGLKLDRI GTMSGLGC	263 (SEQ ID NO: 59)
sp Q09GK2 VNP_PHIOL	---KG	CFGLKLDRI SMSGLGC	164 (SEQ ID NO: 60)
tr D1MZV3 D1MZV3_RHATT	---SG	CFGLKLDRI SMSGLGC	161 (SEQ ID NO: 61)
tr Q7T1M4 Q7T1M4_BOTJR	---KG	CFGLKLDRI GTMSGLGC	221 (SEQ ID NO: 62)
tr Q402A2 Q402A2_PETMA	-----	CFGVKLDRI SMSGLGC	116 (SEQ ID NO: 63)
tr Q402A3 Q402A3_LAMJA	-----	CFGVKLDRI SMSGLGC	148 (SEQ ID NO: 64)
tr Q402A1 Q402A1_9PETR	-----	CFGVKLDRI SMSGLGC	133 (SEQ ID NO: 65)
sp P21805 ANFC_CHICK	---RS	CFGVKLDRI SMSGLGC	22 (SEQ ID NO: 66)
tr A9CDT6 A9CDT6_CHICK	---RS	CFGVKLDRI SMSGLGC	130 (SEQ ID NO: 67)
sp P20968 ANFC_RANCA	---RG	CFGVKLDRI GAFSGLGC	129 (SEQ ID NO: 68)
sp P55208 ANFC_TRISC	---RG	CFGVKLDRI GAMSGLGC	136 (SEQ ID NO: 69)
sp P23259 ANFC_SCYCA	---RG	CFGVKLDRI GAMSGLGC	115 (SEQ ID NO: 70)
sp P41319 ANFC_SQUAC	---RS	CFGLKLDRI GAMSGLGC	135 (SEQ ID NO: 71)
tr Q2MH72 Q2MH72_9CHON	---RG	CFGVKLDRI GAMSGLGC	131 (SEQ ID NO: 72)
tr Q2MH73 Q2MH73_9CHON	---RG	CFGVKLDRI GAMSGLGC	131 (SEQ ID NO: 73)
tr Q2MH71 Q2MH71_9CHON	---RG	CFGVKLDRI GAMSGLGC	131 (SEQ ID NO: 74)
tr Q2MH74 Q2MH74_DASAK	---RG	CFGVKLDRI GAMSGLGC	131 (SEQ ID NO: 75)
tr Q2PF87 Q2PF87_CALMI	---RG	CFGVKLDRI GAMSGLGC	139 (SEQ ID NO: 76)
sp Q80018 ANFC3_ORYLA	---RS	CFGVRLERIGSF SGLGC	112 (SEQ ID NO: 77)
tr Q4ADV1 Q4ADV1_ORYLA	---RS	CFGVRLERIGSF SGLGC	112 (SEQ ID NO: 78)
sp Q805D4 ANFC3_TAKRU	---RS	CFGVRLARIGSF SGLGC	158 (SEQ ID NO: 79)
tr C0H7B0 C0H7B0_SALSA	---RS	CFGVRLERIGSF SGLGC	128 (SEQ ID NO: 80)
tr C1BWD1 C1BWD1_ESOLU	---RS	CFGVRLERIGSF SGLGC	126 (SEQ ID NO: 81)
tr D2KXA3 D2KXA3_ANGJA	---RS	CFGVRLERIGSF SGLGC	128 (SEQ ID NO: 82)
tr B3DJJ2 B3DJJ2_DANRE	---RS	CFGVRLERIGSF SGLGC	128 (SEQ ID NO: 83)
tr Q1XGY8 Q1XGY8_9ACTI	---RS	CFGVRLDRI SMSGLGC	130 (SEQ ID NO: 84)
sp Q8AXR2 ANFC2_ONCMY	---RG	CFGLKLDRI SMSGLGC	131 (SEQ ID NO: 85)
sp Q8AXR3 ANFC1_ONCMY	---RG	CFGLKLDRI SMSGLGC	131 (SEQ ID NO: 86)
tr C1BKS8 C1BKS8_OSMMO	---RG	CFGLKLDRI SMSGLGC	132 (SEQ ID NO: 87)
tr Q805E7 Q805E7_OREMO	---RG	CFGLKLDRI SMSGLGC	131 (SEQ ID NO: 88)
tr C3KH23 C3KH23_ANOFI	---RG	CFGLKLDRI SMSGLGC	131 (SEQ ID NO: 89)
sp Q8AYR6 ANFC1_ORYLA	---RG	CFGLKLDRI SMSGLGC	131 (SEQ ID NO: 90)
sp Q805D6 ANFC1_TAKRU	---RG	CFGLKLDRI SMSGLGC	126 (SEQ ID NO: 91)
sp P18145 ANFC_ANGJA	---RG	CFGLKLDRI GLSGLGC	131 (SEQ ID NO: 92)
tr Q1XGY9 Q1XGY9_9ACTI	---KG	CFGLKLDRI GSI SGLGC	140 (SEQ ID NO: 93)
tr A9CDT5 A9CDT5_CHICK	---RG	CFGLKMDRI GAFSGLGC	123 (SEQ ID NO: 94)
CONSENSUS SEQUENCE	*** : ** : ** : **	CFGXXXXRXXXXSGXGC	(SEQ ID NO: 95)

FIG. 16
Schematic Structure of Natriuretic Peptide



Schematic Structures of Exemplary Fc-NP or NP-Fc Fusion Proteins

FIG. 17A

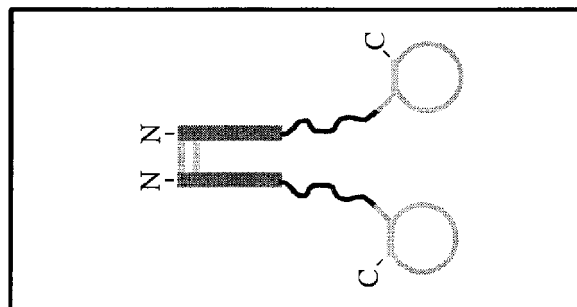


FIG. 17B

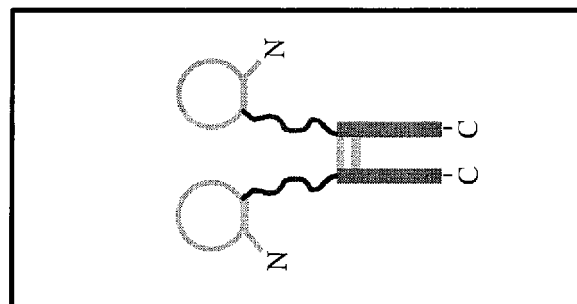


FIG. 17C

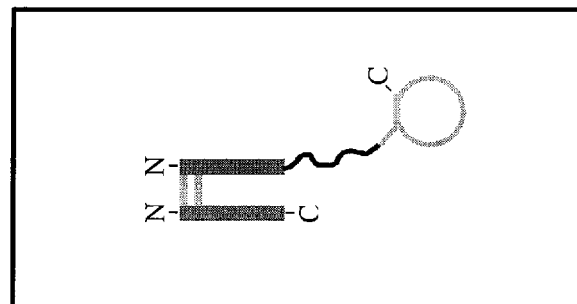


FIG. 17D

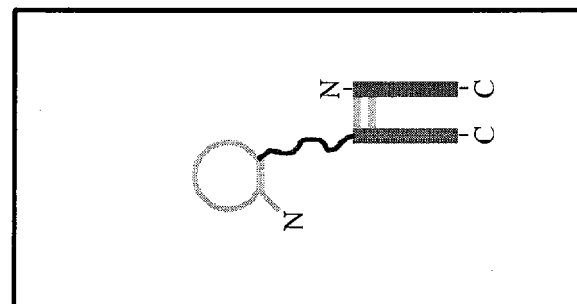


FIG. 17E

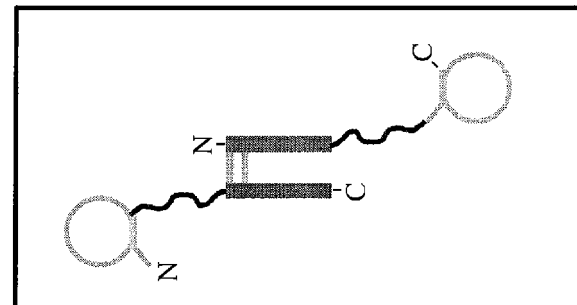


FIG. 18A

NC2st Protein Sequence (With Signal Sequence)

Sequence:

10 20 30 40 50 60
MGVHECPAWL WLLLSLLSLW PGAYAAWSH PQFEQSGGG GENLYFQGG KTHTCPPCPA

70 80 90 100 110 120
PELLGGPSVF LFPPKPKDTL MISRTPEVC VVDVSHEDP EVKFNWYVDG VEVHNAKTKP

130 140 150 160 170 180
REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL

190 200 210 220 230 240
PPSREEMTKN QVSLTCLVKG FYPSDIAVEW ESNQGPENNY KTTPPVLDSD GSFFLYSKLT

250 260 270 280 290 300
VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPKG GGG SGGGSGGGG SGGLSKGCFG

310
LKLDRIQSMG GLGC

(SED ID NO: 501)

Number of amino acids: 314
Molecular weight of monomer: 34053.5

1-25 = Signal peptide
26-27 = Linker
28-35 = Strep-tag II
36-41 = Linker
42-47 = Tobacco etch virus protease cleavage sequence
48-49 = Linker
50-276 = Fc domain of human IgG1
277-292 = Glycine-rich linker
293-314 = C-type natriuretic peptide

FIG. 18B**NC2st Protein Sequence (Without Signal Sequence)**

NC2st (w/o sig. seq.) ASWSHPQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFPPKPD~~TL~~MI~~SR~~TP~~EV~~TCVVDVSHE
DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP~~IE~~KTISKAKGQ
PREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK~~TT~~PPVLDSDGSFFLYSKLTVDKS
RWQQGNVFS~~CS~~VMHEALHNHYTQKSLSLSPGKGGGGSGGGSGGGSGGLSKGCFGLKLD~~RIGSM~~SGGLGC
(SEQ ID NO: 502)

FIG. 18C

NC2st DNA Sequence

ATGGGCGTGACGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTGTGTGGCCTGGCGCCTACGCCGCTCTTTGGAGC
CACCCCCAGTTTGAGCAGTCTGGCGGAGGAGGCGAGAACCTGTACTTTCAGGGCGGCGACAAGACCCACACCTGTCCCCCTTGT
CCTGCCCCCTGAGCTGCTGGGCGGACCCAGCGTGTTCCTGTTCCTCCCAAGCCCAAGGACACCCCTGATGATCAGCCGGACCCCCGAA
GTGACCTGCGTGGTGGTGGACGTGTCCACGAGGACCCCTGAAGTGAAGTTCAATTGTACGTGGACGGCGTGGAGGTGCACAACGCC
AAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGCACCCAGGACTGGCTGAACGGC
AAAGAGTACAAGTGCAAGTCTCCAACAAGGCCCTGCCTGCCCTCCATCGAGAAAACCATCAGCAAGGCCAAGGCCAGCCAGAGAA
CCCCAGGTGTACACCCCTGCCCTCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
AGCGATATCGCCGTGGAGTGGGAGAGCAACGCCAGCCTGAGAACAACTACAAGACCAACCCCTGTGCTGGACAGCGACGGAAGC
TTCTTCCTGTACTCCAACTGACCGTGGACAAGAGCCGGTGGCAGAGGCAACGTGTTTCACTGACGTGACGTGATGCACGAGGCCCTG
CACAAACCACTACACCCAGAAGTCCCTGAGCCTGTCTCCTGGCAAGGGCGGAGGGGGAAGTGGAGCGGAGGAAGCGGGGAGGCGGGA
AGCGGCGGACTGAGCAAGGGCTGCTTCGGCCCTGAAGCTGGACCCGGATCGGCAGCATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO:
801)

FIG. 19A
NC2B Protein Sequences

NC2B (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGLSKGCGFLKLDRI GSM SGLGC (SEQ ID NO: 503)
NC2B (w/o sig. seq.)	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK SLSLSPGKGGGGGGGGGGGGLSKGCGFLKLDRI GSM SGLGC (SEQ ID NO: 504)
D10-NC2 (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSF FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGLSKGCGFLKLDRI GSM SGLGC (SEQ ID NO: 607)
D10-NC2 (w/o sig. seq.)	DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGGSFFLYSKLTVDKSRWQQGNVSCSVMH EALHNHYTQKSLSLSPGKGGGGGGGGGGGGLSKGCGFLKLDRI GSM SGLGC (SEQ ID NO: 608)

FIG. 19B
NC2B DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGTCCTGCCCCCTGAGCTGTCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGTGGACGTGTCCACAGGACCCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCAGCCCCAGAGAACCCAGGTGTACCCCTGCCCCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGCGGACTGAGCAAGGGGTGCTTTCGGCCTGAAGCTGGACCGGATCGGCAGCATGAGCGGCCCTGGGCTGC
TGA (SEQ ID NO: 802)

NC2B-34
(w/o sig. seq.)

[illegible]

FIG. 20B
NC2B-22 DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGCTGCCCTGAGCTGCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGTGTCCACAGGACCCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCAGCCCCAGAACCCAGGTGTACCCCTGCCCCCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCTGCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGACTGAGCAAGGGCTGCTTCGGCCTGAAGCTGGACCGGATCGGCAGC
ATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO: 803)

FIG. 20C
NC2B-28 DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGTCCTGCCCTGAGCTGCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGACGTGTCCACAGGACCCCTGAAGTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGAGGAACAGTACAACAGCACCTACCGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCCAGCCAGAGAACCCAGGTGTACCCCTGCCCCCAAGCCGGGAGGAAATGACCAAGAACCAAGGTGTCCCTGACCTGCCCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTCAAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGAGGAAGTGGCGGAGGCGGACTGAGCAAAGGGCTGCTTCGGCCTGAAG
CTGGACCCGGATCGGCAGCATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO: 804)

FIG. 20D
NC2B-34 DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGCTGCCCCCTGAGCTGTCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGACGTGTCCACAGGAGCCCTGAAGTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCCAGCCAGAGAACCCAGGTGTACCCCTGCCCCCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCCCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGAGGAAGTGGCGGAGGCGGAGCGGCGGAGGGGAGGACTGAGCAAG
GGCTGCTTCGGCCTGAAGCTGGACCGGATCGGCAGCATGAGCGGCCTGGGCTGCTGA (SEQ ID NO: 805)

FIG. 21

NC2 Variants

NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGSGKANKKGLSKGCGGLKLDRI GMSGLGC
(SEQ ID NO: 511)

NC2-KGANKK
(w/o sig. seq.)

DKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANKKGLSKGCGGLKLDRI GMSGLGC (SEQ ID NO: 512)

NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGSGKANQKGLSKGCGGLKLDRI GMSGLGC
(SEQ ID NO: 513)

NC2-KGANQK
(w/o sig. seq.)

DKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANQKGLSKGCGGLKLDRI GMSGLGC (SEQ ID NO: 514)

FIG. 22

NC2 Variants

NC2-CNP53mut2
(w/sig. seq.)

MGVHECPA**WLWLLLSLLSLWP**GAYADKTHTCPPCPAP**ELLG**PSVFLFPPKPKD**TLMIS**RTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHN**AKTKPRE**EQYNSTYRVVSVLTVLHQD**WLN**KEYCKVSNKALPAP**IEKTIS**KAKG
QPREPQVY**YTLPPS**REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK**TTTPV**LDSDGSFFLYSKLTVDK
SRWQQGNVFSC**VMHEALHNHYTQKSLS**SPGKGGGDLQVD**TQSQAAWAQLLQ**EHFNAQQYKGANKKGLSKGC
FG**LKLDRI**GSM**SGLGC** (SEQ ID NO: 515)

NC2-CNP53mut2
(w/o sig. seq.)

DKTHTCPPCPAP**ELLG**PSVFLFPPKPKD**TLMIS**RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN**AKTKPRE**
EQYNSTYRVVSVLTVLHQD**WLN**KEYCKVSNKALPAP**IEKTI**SKAKGQPREPQVY**TLPPS**REEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYK**TTTPV**LDSDGSFFLYSKLTVDKSRWQQGNVFSC**VMHEALHNHYTQK**
SLSLSPGKGGGDLQVD**TQSQAAWAQLLQ**EHFNAQQYKGANKKGLSKGC**FG**LKLDRI**GSM**SGLGC (SEQ ID
NO: 516)

FIG. 23

Fc-CNP53 Constructs

Fc-CNP53-A
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTTLPSSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGC
EGLKLDRIGSASGLGC (SEQ ID NO: 517)

Fc-CNP53-A
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTTLPSSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGCGFLKLDRIGSASGLGC (SEQ ID
NO: 518)

Fc-CNP53-AAA
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTTLPSSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGC
EGLKLDRIGSASGLGC (SEQ ID NO: 519)

Fc-CNP53-AAA
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTTLPSSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGCGFLKLDRIGSASGLGC (SEQ ID
NO: 520)

FIG. 24
NP Multiple Sequence Alignment and CDNP Constructs

Human ANP	SLRRSSCFGGRMDRIGAQSGLGNCNSFRY	(SEQ ID NO: 1)
Rat ANP	SLRRSSCFGGRIDRIGAQSGLGNCNSFRY	(SEQ ID NO: 96)
Urodilatin	TAPRSLRRSSCFGGRMDRIGAQSGLGNCNSFRY	(SEQ ID NO: 2)
Human BNP	SPKMVQSGGCFGRKMDRISSSSSGLGCKVLRRH	(SEQ ID NO: 3)
Rat BNP	SQDSAFRIQERLRNSKMAHSSSSCFGQKIDRIGAVSRGLGCDGLRLF	(SEQ ID NO: 97)
Pig BNP	SPKTMRDSSGCFGRRIDRIGSLGGLGNCVLRRY	(SEQ ID NO: 98)
DNP	EVKYDPFCFCHKIDRINHVSNLGCPSLRDRPRNAPSTSA	(SEQ ID NO: 5)
TNP-C	SDSKIENGCGFGFPLDRIGSVSGLGNCNRIQNPPKKFSGE	(SEQ ID NO: 99)
CDNP	GLSKGCGFGLKLDRI GSMSGLGCPSLRDRPRNAPSTSA	(SEQ ID NO: 100)
	*** : *** * . *** :	
	*** : *** * . *** :	
CDNP-N1 (C7)	GLSKGCGFGLKLDRI GSMSGLGNCNSLRDRPRNAPSTSA	(SEQ ID NO: 101)
CDNP-G1 (C8)	GLSKGCGFGLKLDRI GSMSGLGCGSLRDRPRNAPSTSA	(SEQ ID NO: 102)
CDNP-H1 (C9)	GLSKGCGFGLKLDRI GSMSGLGCHSLRDRPRNAPSTSA	(SEQ ID NO: 103)
CDNP-K1	GLSKGCGFGLKLDRI GSMSGLGCKSLRDRPRNAPSTSA	(SEQ ID NO: 104)
CDNP-Z1 (Z=hydroxyproline)	GLSKGCGFGLKLDRI GSMSGLGCGZSLRDRPRNAPSTSA	(SEQ ID NO: 105)
CDNP-S3	GLSKGCGFGLKLDRI GSMSGLGCPSSRDRPRNAPSTSA	(SEQ ID NO: 106)
CDNP-A4	GLSKGCGFGLKLDRI GSMSGLGCPSLADPRNAPSTSA	(SEQ ID NO: 107)
CDNP-A5	GLSKGCGFGLKLDRI GSMSGLGCPSLRAPRNPAPSTSA	(SEQ ID NO: 108)
CDNP-S3A4 (C12)	GLSKGCGFGLKLDRI GSMSGLGCPSSADPRNPAPSTSA	(SEQ ID NO: 109)
CDNP-A4A5	GLSKGCGFGLKLDRI GSMSGLGCPSLAAPRNPAPSTSA	(SEQ ID NO: 110)
CDNP-S3A5 (C11)	GLSKGCGFGLKLDRI GSMSGLGCPSSRAPRNPAPSTSA	(SEQ ID NO: 111)
CDNP-(A17)S3A5	GLSKGCGFGLKLDRI GSASGLGCPSSRAPRNPAPSTSA	(SEQ ID NO: 112)
CDNP-S3A4A5 (C10)	GLSKGCGFGLKLDRI GSMSGLGCPSSAAPRNPAPSTSA	(SEQ ID NO: 113)
CDNP-(A17)S3A4A5	GLSKGCGFGLKLDRI GSASGLGCPSSAAPRNPAPSTSA	(SEQ ID NO: 114)
CDNP-S3A4A5R6 (C13)	GLSKGCGFGLKLDRI GSMSGLGCPSSAARRNPAPSTSA	(SEQ ID NO: 115)
CDNP-S3A4A5S7 (C14)	GLSKGCGFGLKLDRI GSMSGLGCPSSAAPSPNAPSTSA	(SEQ ID NO: 116)
DNP TAIL		
CONSENSUS SEQUENCE FOR DNP C-TERMINAL TAIL	PSLRDRPRNAPSTSA	(SEQ ID NO: 117)
	XSXXXXPNAPSTSA	(SEQ ID NO: 118)

FIG. 25A

Exemplary Constructs Having N-terminal NP fused to C-terminal Fc Domain

CNP-16AAlinker-Fc-His₁₀
(NC1) GLSKGCFGLKLDRI~~GSMSGLGCGGGSGGGSGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP~~

PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDG
GSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ
ID NO: 521)

CNP-6AAlinker-Fc-His₁₀
(NC3) GLSKGCFGLKLDRI~~GSMSGLGCGGGSGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK~~

AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 522)

CNP-6AAlinker-Fc

GLSKGCFGLKLDRI~~GSMSGLGCGGGSGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK~~
AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 523)

CDNP-Fc

GLSKGCFGLKLDRI~~GSMSGLGCPSLRDRPNAPSTISADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP~~
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 524)

CDNP-A17saa-Fc

GLSKGCFGLKLDRI~~GSASGLGCPSSAAPRPNAPSTISADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP~~
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 525)

CDNP-A17sra-Fc

GLSKGCFGLKLDRI~~GSASGLGCPSSRAPRPNAPSTISADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP~~
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 526)

FIG. 25B

NC1 DNA Sequence

ATGGGCGTGACGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTGTGGCCCTGGCGCCTACGCCGGCCCTGAGCAAAG
GGCTGCTTCGGCCTGAAGCTGGACCGGATCGGCAGCATGTCTGGCCTGGCTGTGGAGCGGAGGATCTGGCGCGGAGGAAGTGGC
GGAGGGCAGCGGCGATAAGACCCACACCTGTCCCCCTTGTCTGCCCCTGAGCTGTCTGGGGGACCCAGCGTGTCTCTGTTCCTCC
CCAAAGCCCCAAGGACACCCCTGATGATCAGCCGGACCCCCGAAGTGACCTGCTGGTGGTGTGCCACGAGGACCCCTGAAGTG
AAGTTCAATTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTG
GTGTCCGTGCTGACCGTGTGCAACGAGGACTGGCTGAACGGCAAAAGATACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCC
ATCGAGAAAACCATCAGCAAGGCCAAGGCCAGCCAGAGAACCCAGGTGTACACCCCTGCCCCAGCCGGAGGAAATGACCAAAG
AACCAGGTGTCCCTGACCTGCCCTGGTGAAGGGCTTCTACCCAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAAC
AACTACAAGACCACCCCCTGTGTGTGACAGCGACGGCAGCTTCTCTGTACTCCAAACTGACCGTGGACAAAGAGCCGGTGGCAG
CAGGGCAACGTTTTCAGCTGCAGCGTGTATGCACGAGGCCCTGCACAACCACTACACCCAGAAAGTCCCTGAGCCTGTCTCTCTGGCAAAG
GGCGGCGAGAACCTGTACTTTCAGGGCAGCCACCACCATCACCATCATCACTGA (SEQ ID NO: 806)

FIG. 26
Human CNP22 and Point Mutations at Position 17

CNP22	GLSKGCFGLKLDRI ^{MS} GLGC	(SEQ ID NO: 4)
CNP-F17 (C15)	GLSKGCFGLKLDRI ^{GS} FSGLGC	(SEQ ID NO: 119)
CNP-L17 (C16)	GLSKGCFGLKLDRI ^{GS} <u>I</u> SGLGC	(SEQ ID NO: 120)
CNP-I17 (C17)	GLSKGCFGLKLDRI ^{GS} <u>I</u> SGLGC	(SEQ ID NO: 121)
CNP-T17 (C18)	GLSKGCFGLKLDRI ^{GS} <u>TS</u> GLGC	(SEQ ID NO: 122)
CNP-V17 (C19)	GLSKGCFGLKLDRI ^{GS} <u>V</u> SGLGC	(SEQ ID NO: 123)
CNP-A17 (C1)	GLSKGCFGLKLDRI ^{GS} <u>A</u> SGLGC	(SEQ ID NO: 124)
CNP-S17	GLSKGCFGLKLDRI ^{GS} <u>S</u> SGLGC	(SEQ ID NO: 125)
CNP-E17	GLSKGCFGLKLDRI ^{GS} <u>E</u> SGLGC	(SEQ ID NO: 156)
CNP-R17	GLSKGCFGLKLDRI ^{GS} <u>R</u> SGLGC	(SEQ ID NO: 157)
CNP-Y17	GLSKGCFGLKLDRI ^{GS} <u>Y</u> SGLGC	(SEQ ID NO: 158)
CONSENSUS:	GLSKGCFGLKLDRI ^{GS} <u>X</u> SGLGC	(SEQ ID NO: 126)

FIG. 27

CNP Variants

CNP22		GLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 4)
CNP37	QEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 127)	
E6PGCNP37	EEEEEPGQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 128)	
C1 (E6)	EEEEESGGGGSGGGSGGGGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 129)	
C2 (E6)	EEEEEEASTSPANPQPAASSPGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 130)	
C3 (E6)	EEEEEEPSSAAPQPNAPSTSAGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 131)	
C4 (E6)	EEEEESGGGGSGGGKANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 132)	
C5 (E6)	EEEEESGGGGSGGGQGANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 133)	
C6 (E6)	EEEEESGGGGSGGGKANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 134)	
C7 (E6)	EEEEESGGGGSGGGKANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 135)	
C8 (E6)	EEEEESGGGGSGGGQGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 136)	
C9 (E6)	EEEEESGGGGSGGGKANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 137)	
C10 (E6)	EEEEESGGGGSGGGQGANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 138)	
C11 (E6)	EEEEESGGGGSGGGQGANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 139)	
D6CNP37	DDDDDDQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 140)	
C1 (D6)	DDDDDDSGGGSGGGSGGGGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 141)	
C2 (D6)	DDDDDDASTSPANPQPAASSGGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 142)	
C3 (D6)	DDDDDDGSSAAPQPNAPSTSAGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 143)	
C4 (D6)	DDDDDDSGGGSGGGKANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 144)	
C5 (D6)	DDDDDDSGGGSGGGQGANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 145)	
C6 (D6)	DDDDDDSGGGSGGGKANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 146)	
D6-14AAlinker-CNP	DDDDDDSGGGSGGGSGGGGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 147)	
CNP-14AAlinker-D6	GLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 148)	
CNP-Nterm1	GSSAAPRPNAPSTSAGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 149)	
CNP-Nterm2	ASTSPANPRPAASSGGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 150)	

FIG. 28A
Additional CNP Variants

GDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1001)
PDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1002)
MDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1003)
DLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1004)
LRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1005)
RVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1006)
VDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1007)
DTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1008)
TKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1009)
KSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1010)
SRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1011)
RAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1012)
AAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1013)
AWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1014)
WARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1015)
ARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1016)
RLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1017)
LLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1018)
LQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1019)
EHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1020)
HPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1021)
PNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1022)
NARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1023)
ARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1024)
RKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1025)
KYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1026)
YKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1027)
KGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1028)
GANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1029)
ANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1030)
NKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1031)

FIG. 28B

KKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1032)
KGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1033)
LSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1034)
SKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1035)
KGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1036)
GCFLKLDRIGSMSGLGC	(SEQ ID NO: 1037)
QEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1038)
PQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1039)
MQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1040)
GQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1041)
GQEHPNARKYKGANPKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1042)
GQEHPNARKYKGANQKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1043)
GQEHPNARKYKGANQQGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1044)
GQEHPNARKYKGANKPKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1045)
GQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1046)
PGQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1047)
MGQEHPNARKYKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1048)
GANRRGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1049)
GANRRGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1050)
PGANRRGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1051)
MGANRRGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1052)
GHKSEVAHRFKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1053)
GHKSEVAHRFKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1054)
PGHKSEVAHRFKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1055)
MGHKSEVAHRFKGANKKKGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1056)
RGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1057)
ERGLSRGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1058)
GANQQGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1059)
GANRRGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1060)
GANPRGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1061)
GANSSGLSKGCFGLKLDRIGSMSGLGC	(SEQ ID NO: 1062)

FIG. 28C

	GANPRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1063)
	GANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1064)
	GANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1065)
	GANS SGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1066)
	AAWARLLQEHPNAGLSK GCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1067)
	AAWARLLQEHPNARGLSK GCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1068)
	DLRVDTKSRAAWARGLSK GCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1069)
	GQEHPNARKYKGANPKGLSK GCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1070)
	GQEHPNARKYKGANQKGLSK GCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1071)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1072)
	ERGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1073)
	RGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1074)
	GLSRGCFGLRLDRI GSM SGLGC	(SEQ ID NO: 1075)
	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1076)
	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1077)
	RLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1078)
	ELSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1079)
	GLSKRCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1080)
	GLSKQCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1081)
	GLSKSCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1082)
	GLSKGCFGLKLDRI SSMSGLGC	(SEQ ID NO: 1083)
	GLSKGCFGLKLDRI NSMSGLGC	(SEQ ID NO: 1084)
	GLSKGCFGLKLDRI RSMSGLGC	(SEQ ID NO: 1085)
	GLSKGCFGLKLDRI XSMSGLGC	(SEQ ID NO: 1086)
	GLSKGCFGLKLDRI GSM SSSLGC	(SEQ ID NO: 1087)
	GLSKGCFGLKLDRI GSM SRLGC	(SEQ ID NO: 1088)
	GLSKGCFGLKLDRI GSM SNLGC	(SEQ ID NO: 1089)
	GLSKGCFGLKLDRI GSM SGLSC	(SEQ ID NO: 1090)
	GLSKGCFGLKLDRI GSM SGLTC	(SEQ ID NO: 1091)
	GLSKGCFGLKLDRI GSM SGLRC	(SEQ ID NO: 1092)
	GLSKGCXFGLKLDRI GSM SGLGC	(SEQ ID NO: 1093)

(X: D-Phe)

(X: 3-amino-2-phenylpropionic acid)

(X: Cit)

(X: [CH₂NH]bond)

FIG. 28D

(X: N-Me-Phe)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1094)
(X: t-Bu-Gly)	GLSKGCFXLKLDRI GSM SGLGC	(SEQ ID NO: 1095)
(X: NHCH ₂ CH (Ph) CO)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1096)
	GQPREPQVYTLPPSGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1097)
	GERAFKAWAVARLSQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1098)
	GQHKDDNPNLPRGANPRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1099)
	GHHSEQHHPHGANQQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1100)
	GAHHPHEHDTHGANOQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1101)
	FGIPMDRIGRNPRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1102)
	GKRTGQYKLGSKTGP GPKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1103)
	SPKMVQSGGCFGLKLDRI GSM SGLGCKVLRH	(SEQ ID NO: 1104)
	GQPREPQVYTGANOQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1105)
	GVPQVSTGTGANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1106)
	GQPSSSQSTGANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1107)
	GSTGQWHSESGANOQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1108)
	GQTHSSGTQSGANOQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1109)
	GSSSSSSSSSGANOQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1110)
(X ₁ : [CH ₂ NH] bond; X ₂ and X ₃ : N-Me-Leu)	GLSKGCX ₁ FGX ₂ KLDRI GSM SGLGC	(SEQ ID NO: 1111)
(X ₁ and X ₂ : N-Me-Leu)	GLSKGCFGX ₁ KLDRI GSM SGLGC	(SEQ ID NO: 1112)
(X ₁ , X ₂ , and X ₃ : N-Me-Leu)	GLSKGCFGX ₁ KX ₂ DRIGSM SGLGC	(SEQ ID NO: 1113)
(X ₁ and X ₂ : N-Me-Leu)	GLSKGCFGX ₁ KX ₂ DRIGSM SGLGC	(SEQ ID NO: 1114)
	GLSRGCYGLKLDRI GSM SGLGC	(SEQ ID NO: 1115)
	GLSRGCFVLKLDRI GSM SGLGC	(SEQ ID NO: 1116)
	GLSRGCFSLKLDRI GSM SGLGC	(SEQ ID NO: 1117)
	GLSRGCFTLKLDRI GSM SGLGC	(SEQ ID NO: 1118)
	GLSRGCFGTKLDRI GSM SGLGC	(SEQ ID NO: 1119)
	GLSRGCFGLKLDRI RSM SGLGC	(SEQ ID NO: 1120)
	GLSRGCFGLKLDRI XSM SGLGC	(SEQ ID NO: 1121)
(X: Cit)	GLSRGCFGLKLDRI GSVSGLGC	(SEQ ID NO: 1122)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1123)
(X: t-Bu-Ala)	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1124)

FIG. 30
CNP variants having Point Mutations at Position 17

CNP-X17	GLSKG CFGLKLD RIGSX SGLGC	(SEQ ID NO: 126)
CNP-F17	GLSKG CFGLKLD RIGSF SGLGC	(SEQ ID NO: 119)
CNP-L17	GLSKG CFGLKLD RIGSL SGLGC	(SEQ ID NO: 120)
CNP-I17	GLSKG CFGLKLD RIGSI SGLGC	(SEQ ID NO: 121)
CNP-T17	GLSKG CFGLKLD RIGST SGLGC	(SEQ ID NO: 122)
CNP-E17	GLSKG CFGLKLD RIGSE SGLGC	(SEQ ID NO: 156)
CNP-R17	GLSKG CFGLKLD RIGSR SGLGC	(SEQ ID NO: 157)
CNP-Y17	GLSKG CFGLKLD RIGSY SGLGC	(SEQ ID NO: 158)
CNP-C17	GLSKG CFGLKLD RIGSC SGLGC	(SEQ ID NO: 159)
CNP-P17	GLSKG CFGLKLD RIGSP SGLGC	(SEQ ID NO: 160)
CNP-D17	GLSKG CFGLKLD RIGSD SGLGC	(SEQ ID NO: 161)
CNP37-X17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSX SGLGC	(SEQ ID NO: 162)
CNP37-F17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSF SGLGC	(SEQ ID NO: 163)
CNP37-L17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSL SGLGC	(SEQ ID NO: 164)
CNP37-I17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSI SGLGC	(SEQ ID NO: 165)
CNP37-T17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGST SGLGC	(SEQ ID NO: 166)
CNP37-E17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSE SGLGC	(SEQ ID NO: 167)
CNP37-R17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSR SGLGC	(SEQ ID NO: 168)
CNP37-Y17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSY SGLGC	(SEQ ID NO: 169)
CNP37-C17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSC SGLGC	(SEQ ID NO: 170)
CNP37-P17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSP SGLGC	(SEQ ID NO: 171)
CNP37-D17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSD SGLGC	(SEQ ID NO: 172)

FIG. 31A
Additional CNP variants having Point Mutations at Position 17

KA1-X17	<u>HGPQQEHPN</u> ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 173)
KA2-X17	SGGGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 174)
KA3-X17	GGGHGPQGEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 175)
KA4-X17	GGSGGGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 176)
KA5-X17	SGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 177)
KA6-X17	<u>HGPQQEHPN</u> ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 178)
KA7-X17	GGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 179)
KA8-X17	GGGHGPQGEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 180)
KB1-X17	<u>HKLRGQEHPN</u> ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 181)
KB2-X17	GGGHKLRCQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 182)
KB3-X17	<u>HKLRGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC</u>	(SEQ ID NO: 183)
KB4-X17	<u>GGGHKLRCGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC</u>	(SEQ ID NO: 184)
PGCNP37-X17	PGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 185)
KA1(E6)-X17	EEEEEEHGPQQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 186)
KA2(E6)-X17	EEEEEESGGGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 187)
KA3(E6)-X17	EEEEEEGGGHGPQGEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 188)
KA4(E6)-X17	EEEEEEGGSGGGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 189)
KA5(E6)-X17	EEEEEESSGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 190)
KA6(E6)-X17	EEEEEEHGPQQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 191)
KA7(E6)-X17	EEEEEEGGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 192)
KA8(E6)-X17	EEEEEEGGGHGPQGEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 193)
KB1(E6)-X17	EEEEEEHKLRGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 194)
KB2(E6)-X17	EEEEEEGGGHKLRCQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 195)
KB3(E6)-X17	EEEEEEHKLRGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 196)
KB4(E6)-X17	EEEEEEGGGHKLRCGSGGGSGGGSGGGKGANCKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 197)
E6PGCNP37-X17	EEEEEEPGQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 198)

FIG. 31B

Additional CNP variants having Point Mutations at Position 17

C1 (E6) -X17	EEEEEESSGGGSGGGGGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 199)
C2 (E6) -X17	EEEEEEASTSPANPQPAASSPGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 200)
C3 (E6) -X17	EEEEEEPSAAPQPNAPSTSAGLSKGCFLKLDRIGSXSLGC	(SEQ ID NO: 201)
C4 (E6) -X17	EEEEEESSGGGSGGGKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 202)
C5 (E6) -X17	EEEEEESSGGGSGGGQGANQQGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 203)
C6 (E6) -X17	EEEEEESSGGGSGGGKGANQKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 204)
C7 (E6) -X17	EEEEEESSGGGSGGGKGANQKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 205)
C8 (E6) -X17	EEEEEESSGGGSGGGQGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 206)
C9 (E6) -X17	EEEEEESSGGGSGGGKGANQQGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 207)
C10 (E6) -X17	EEEEEESSGGGSGGGQGANQKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 208)
C11 (E6) -X17	EEEEEESSGGGSGGGQGANQKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 209)
D6CNP37-X17	DDDDDDQEHPNARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 210)
C1 (D6) -X17	DDDDDDSSGGGSGGGGGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 211)
C2 (D6) -X17	DDDDDDASTSPANPQPAASSGGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 212)
C3 (D6) -X17	DDDDDDGSSAAPQPNAPSTSAGLSKGCFLKLDRIGSXSLGC	(SEQ ID NO: 213)
C4 (D6) -X17	DDDDDDSSGGGSGGGKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 214)
C5 (D6) -X17	DDDDDDSSGGGSGGGQGANQQGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 215)
C6 (D6) -X17	DDDDDDSSGGGSGGGKGANQKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 216)
D6-14AAlinker-CNP-X17	DDDDDDSSGGGSGGGGGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 217)
CNP-14AAlinker-D6-X17	GLSKGCFGLKLDRIGSXSLCGGGGGGGGGDDDD	(SEQ ID NO: 218)
CNP-Nterm1-X17	GSSAAPRPNAPSTSAGLSKGCFLKLDRIGSXSLGC	(SEQ ID NO: 219)
CNP-Nterm2-X17	ASTSPANRPRAASSGGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 220)

FIG. 32
CNP variants having M17L

KA1 (E6) -L17	EEEEEEHGPQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 221)
KA2 (E6) -L17	EEEEEESSGGGQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 222)
KA3 (E6) -L17	EEEEEEGGGHGPQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 223)
KA4 (E6) -L17	EEEEEEGGSGGGQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 224)
KA5 (E6) -L17	EEEEEESSGGSGGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 225)
KA6 (E6) -L17	EEEEEEHGPQSGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 226)
KA7 (E6) -L17	EEEEEEGGSGGGSGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 227)
KA8 (E6) -L17	EEEEEEGGGHGPQSGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 228)
KB1 (E6) -L17	EEEEEEHKLRGQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 229)
KB2 (E6) -L17	EEEEEEGGGHKLRGQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 230)
KB3 (E6) -L17	EEEEEEHKLRGSGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 231)
KB4 (E6) -L17	EEEEEEGGCHKLRGSGGGSGGGKGAN KK GLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 232)
E6PGCNP37-L17	EEEEEPGQGEHPNARKYKGANKKKGLSKGCFGLKLDRI GS SLGLGC	(SEQ ID NO: 233)

FIG. 33A

NC2st-X17 and NC2B-X17 Protein Sequences

NC2st-X17 (w/ sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYAASWSHPQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGSG GLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 527)
NC2st-X17 (w/o sig. seq.)	ASWSHPQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFPKPKDTLMISRTPEVTCVVVDVSH DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGSFFLYSKLTVDKS RWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGSGGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 528)
NC2B-X17 (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPKPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGSGGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 529)
NC2B-X17 (w/o sig. seq.)	DKTHTCPPCPAPELLGGPSVFLFPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK SLSLSPGKGGGGGGGGGGGGSGGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 530)

NC2B-22-X17
(w/sig. seq.

NC2B-22-X17
(w/o sig. seq.)

NC2B-28-X17
(w/sig. seq.)

NC2B-28-X17
(w/o sig. seq.)

NC2B-34-X17
(w/sig. seq.)

NC2B-34-X17
(w/o sig. seq.)

[illegible]

FIG. 33C
NC2-X17 Variants

NC2-KGANKK-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIGSXSLGCG
(SEQ ID NO: 537)

NC2-KGANKK-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID NO: 538)

NC2-KGANQK-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIGSXSLGCG
(SEQ ID NO: 539)

NC2-KGANQK-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID NO: 540)

NC2-CNP53mut2-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKG
FGLKLDRIGSXSLGCG (SEQ ID NO: 541)

NC2-CNP53mut2-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID
NO: 542)

FIG. 33D

Fc-CNP53-X17 Constructs

Fc-CNP53-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSRREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSVMHREALHNHYTQKSLSLSPGKGGGDLRVDITKSRAAWARLLQEHHPNARKYKGANKGLSKGC
EGLKLDRIGSXSGLGCS (SEQ ID NO: 543)

Fc-CNP53-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHREALHNHYTQK
SLSLSPGKGGGDLRVDITKSRAAWARLLQEHHPNARKYKGANKGLSKGCGFLKLDRIGSXSGLGCS (SEQ ID
NO: 544)

Fc-CNP53-AA-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSRREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSVMHREALHNHYTQKSLSLSPGKGGGDLRVDITKSRAAWARLLQEHHPNARKYKGANAAGLSKGC
EGLKLDRIGSXSGLGCS (SEQ ID NO: 545)

Fc-CNP53-AA-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHREALHNHYTQK
SLSLSPGKGGGDLRVDITKSRAAWARLLQEHHPNARKYKGANAAGLSKGCGFLKLDRIGSXSGLGCS (SEQ ID
NO: 546)

FIG. 33E

Constructs Having N-terminal NP-X17 fused to C-terminal Fc Domain

CNP-X17-16AAlinker-Fc-His ₁₀ (NC1)	GLSKGCFGLKLDRIGSXSGLGCGGGGGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 547)
CNP-X17-6AAlinker-Fc-His ₁₀ (NC3)	GLSKGCFGLKLDRIGSXSGLGCGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 548)
CNP-X17-6AAlinker-Fc	GLSKGCFGLKLDRIGSXSGLGCGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 549)
CDNP-X17-Fc	GLSKGCFGLKLDRIGSXSGLGCPSLRDRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 550)
CDNP-X17-saa-Fc	GLSKGCFGLKLDRIGSXSGLGCPSSAAPRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 551)
CDNP-X17-sra-Fc	GLSKGCFGLKLDRIGSXSGLGCPSSRAPRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 552)

FIG. 34A NC2 Variants

NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIQSMGSLGC
(SEQ ID NO: 511)

NC2-KGANKK
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIQSMGSLGC (SEQ ID NO: 512)

NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIQSMGSLGC
(SEQ ID NO: 513)

NC2-KGANQK
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIQSMGSLGC (SEQ ID NO: 514)

NC2-CNP53mut2
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGC
FGLKLDRIQSMGSLGC (SEQ ID NO: 515)

NC2-CNP53mut2
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCFGLKLDRIQSMGSLGC (SEQ ID
NO: 516)

FIG. 34B D10-NC2 Variants

D10-NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSMGSLGC (SEQ ID NO: 553)

D10-NC2-KGANKK
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 554)

D10-NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSMGSLGC (SEQ ID NO: 555)

D10-NC2-KGANQK
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 556)

D10-NC2-CNP53mut2
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 557)

D10-NC2-CNP53mut2
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI GSMGSLG
C (SEQ ID NO: 558)

FIG. 34C
NC2-F17 Variants

NC2-KGANKK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQSFSGLGC
(SEQ ID NO: 559)

NC2-KGANKK-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID NO: 560)

NC2-KGANQK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQSFSGLGC
(SEQ ID NO: 561)

NC2-KGANQK-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID NO: 562)

NC2-CNP53mut2-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGC
FGLKLDRIQSFSGLGC (SEQ ID NO: 563)

NC2-CNP53mut2-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID
NO: 564)

FIG. 34D
D10-NC2-F17 Variants

D10-NC2-KGANKK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTI SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRI
GSFSGLGC (SEQ ID NO: 565)

D10-NC2-KGANKK-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTI SKAKGQPREPQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRI GSFSGLGC (SEQ ID NO: 566)

D10-NC2-KGANQK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTI SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGSGKANKQKGLSKGCFGLKLDRI
GSFSGLGC (SEQ ID NO: 567)

D10-NC2-KGANQK-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTI SKAKGQPREPQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGSGGSGKANKQKGLSKGCFGLKLDRI GSFSGLGC (SEQ ID NO: 568)

D10-NC2-CNP53mut2-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTI SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI GSFSGLGC (SEQ ID NO: 569)

D10-NC2-CNP53mut2-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTI SKAKGQPREPQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQLLEHPNAQQYKANKKGLSKGCFGLKLDRI GSFSGLGC
(SEQ ID NO: 570)

FIG. 34E
NC2-L17 Variants

NC2-KGANKK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKG
QPREPQVY**TLPP**SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGSGKANGKGLSKGC**FGLKLD**RIGSL**SG**LG
(SEQ ID NO: 571)

NC2-KGANKK-L17
(w/o sig. seq.)

DKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKGQPREPQVY**TLPP**SREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**SRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANGKGLSKGC**FGLKLD**RIGSL**SG**LG (SEQ ID NO: 572)

NC2-KGANQK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKG
QPREPQVY**TLPP**SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGSGKANGKGLSKGC**FGLKLD**RIGSL**SG**LG
(SEQ ID NO: 573)

NC2-KGANQK-L17
(w/o sig. seq.)

DKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKGQPREPQVY**TLPP**SREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**SRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANGKGLSKGC**FGLKLD**RIGSL**SG**LG (SEQ ID NO: 574)

NC2-CNP53mut2-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKG
QPREPQVY**TLPP**SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGDLQVDTQ**SQA**AWAQL**LQ**EH**PN**AQQYKGANKKGLSKGC
FGLKLDRIGSL**SG**LG (SEQ ID NO: 575)

NC2-CNP53mut2-L17
(w/o sig. seq.)

DKTHTCPAPELLGGPSVFLFPPKPCDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTV**LHQD**WLN**GEYKCKVSN**KALPAPIEK**TS**SKAKGQPREPQVY**TLPP**SREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYK**TTTP**PVLDSDGSFFLYSKLTV**DK**SRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGKGGGDLQVDTQ**SQA**AWAQL**LQ**EH**PN**AQQYKGANKKGLSKGC**FGLKLD**RIGSL**SG**LG (SEQ ID
NO: 576)

FIG. 34F
D10-NC2-L17 Variants

D10-NC2-KGANKK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGGGSGGSGKGGKGLSKGCFGLKLDRI
GSLSLGLGC (SEQ ID NO: 577)

D10-NC2-KGANKK-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGGGSGGSGKGGKGLSKGCFGLKLDRI (SEQ ID NO: 578)

D10-NC2-KGANQK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGGGSGGSGKGGKGLSKGCFGLKLDRI
GSLSLGLGC (SEQ ID NO: 579)

D10-NC2-KGANQK-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGGGSGGSGKGGKGLSKGCFGLKLDRI (SEQ ID NO: 580)

D10-NC2-CNP53mut2-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI (SEQ ID NO: 581)

D10-NC2-CNP53mut2-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKGGKGLSKGCFGLKLDRI (SEQ ID NO: 582)

FIG. 34G
NC2-R17 Variants

NC2-KGANKK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRIGSSLGCG
(SEQ ID NO: 583)

NC2-KGANKK-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRIGSSLGCG (SEQ ID NO: 584)

NC2-KGANQK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRIGSSLGCG
(SEQ ID NO: 585)

NC2-KGANQK-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRIGSSLGCG (SEQ ID NO: 586)

NC2-CNP53mut2-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHPNAAQQYKGANKKGLSKG
FGLKLDRIGSRLGCG (SEQ ID NO: 587)

NC2-CNP53mut2-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHPNAAQQYKGANKKGLSKGCFGLKLDRIGSSLGCG (SEQ ID
NO: 588)

FIG. 34H D10-NC2-R17 Variants

D10-NC2-KGANKK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSRSLGCG (SEQ ID NO: 589)

D10-NC2-KGANKK-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRIIGSRSLGCG (SEQ ID NO: 590)

D10-NC2-KGANQK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSRSLGCG (SEQ ID NO: 591)

D10-NC2-KGANQK-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRIIGSRSLGCG (SEQ ID NO: 592)

D10-NC2-CNP53mut2-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKQ
ANKKGLSKGCFGLKLDRIIGSRSLGCG (SEQ ID NO: 593)

D10-NC2-CNP53mut2-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRIIGSRSLG
C (SEQ ID NO: 594)

FIG. 34I
NC2-Y17 Variants

NC2-KGANKK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWP
GAYADKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 595)

NC2-KGANKK-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 596)

NC2-KGANQK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWP
GAYADKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 597)

NC2-KGANQK-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 598)

NC2-CNP53mut2-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWP
GAYADKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGDLQVDTQSQAAWAQLLQEH
PNAQQYKGANKKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 599)

NC2-CNP53mut2-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVF
LFPKPCKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTI
SKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGDLQVDTQSQAAWAQLLQEH
PNAQQYKGANKKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 600)

FIG. 34J D10-NC2-Y17 Variants

D10-NC2-KGANKK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 601)

D10-NC2-KGANKK-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 602)

D10-NC2-KGANQK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 603)

D10-NC2-KGANQK-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 604)

D10-NC2-CNP53mut2-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI (SEQ ID NO: 605)

D10-NC2-CNP53mut2-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI (SEQ ID NO: 606)