

NPP1 (wild-type)

MERDGCAGGGSRGGEGRAPREGPAGNGRDRGRSHAAEAPGDPQAAASLLAPMDVGEEPLEKAARA
RTAKDPNTYKVLSLVLSVCVLTTILGCIFGLK**PSCAKE**VKSCKGRCFERTFGNCRCDAACVELGNCCLDYQET
CIEPEHIWTCNKFRCGEKRLTRSLCACSDDKDKGDCCINYSSVCQGEKSWVEEPCESINEQCP**AGFETP**
PTLLFSLDGFRAEYLHTWGGLLPVISKLKKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDP
KMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEERILAV
LQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMLMDGLKELNLHRCLNLILISD
HGMEQGSCKKYIYNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFKPYLKHF
LPKRLHFAKSDRIEPLTFYLDPQWQLALNPSERKYCGSGFHGSDNVFSNMQALFVGYGPGFKHGIEADTF
ENIEVYNLMCDLLNLTPAPNNGTHGSLNHLLKNPVYTPKHPKEVHPLVQCPFTRNPRDNLGCSCNPSILPI
EDFQTQFNLTVAEEKIHKETLPYGRPRVLQKENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTE
DFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHD
TLLRKYAEERNGVNVVSGPVDFDYDGRCDSLENLRQKRRVIRNQEILIPTHFFIVLTSCKDTSQTPLHCENL
DTLAFILPHRTDNSESCVHGKHDSSWVEELMLHRARITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFSQ
ED (SEQ ID NO:1)

Fig. 1

sssNPP1 (NPP1 catalytic domain with no TAG)

AGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDN
KMYDPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPF
EERILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMLMDGLKELNLHRCL
NLILISDHGMEQGSCKKYIYNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFK
PYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSERKYCGSGFHGSDNVFSNMQALFVGYGPGFKHG
IEADTFENIEVYNLMCDLLNLTPAPNNGTHGSL (SEQ ID NO:2)

Fig. 2

TAGsssNPP1 (N-terminus D8)

IGVLLTQRTLLSLVLALLFPSMASM**DDDDDDDD**AGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCG
TYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPWVTAKY
QGLKSGTFFWPGSDVEINGIFPDYKMYNGSVPFEERILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYG
PVSSEVIKALQRVDGMVGMLMDGLKELNLHRCLNLILISDHGMEQGSCCKYIYLNKYLGDVKNIKVIYGPA
ARLRPSDVPDKYYSFNYESGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSE
RKYCGSGFHGSDNVFSNMQALFVGYPGPFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSL (SEQ
ID NO:3)

Fig. 3

TAGsssNPP1 (C-terminus D10)

IGVLLTQRTLLSLVLALLFPSMASMAGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCGTYTKNMRPV
YPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPWVTAKYQGLKSGTFF
WPGSDVEINGIFPDYKMYNGSVPFEERILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKAL
QRVDGMVGMLMDGLKELNLHRCLNLILISDHGMEQGSCCKYIYLNKYLGDVKNIKVIYGPAARLRPSDVP
DKYYSFNYESGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKRYCGSGFH
GSDNVFSNMQALFVGYPGPFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSL**DDDDDDDDDD**
(SEQ ID NO:4)

Fig. 4

TAGssNPP1 (N-terminus D8)

ATGGGTGTA CTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCAAGCATGGCGAGCA
TGGATGACGATGATGACGACGATGACGCAGGGTTTGAAACGCCTCCTACACTCTTGTTTCTTTGGATGGATT
CAGGGCAGAATATTTGCACACTTGGGGTGGACTTCTTCCTGTTATTAGCAAACCTCAAAAAATGTGGAACATAT
ACTAAAAACATGAGACCGGTGTATCCAACAAAACTTTCCCAATCACTACAGCATTGTCACCGGATTGTATCC
AGAATCTCATGGCATAATCGACAATAAGATGTATGATCCCAAAATGAATGCTTCCTTTTCACTTAAAAGTAAAG
AGAAATTTAATCCGGAGTGGTACAAAGGAGAACCAATTTGGGTACAGCTAAGTATCAAGGCCTCAAGTCTG
GCACATTTTTCTGGCCAGGATCAGATGTGGAAATTAACGGAATTTCCAGACATCTATAAAATGTATAATGGT
TCAGTGCCATTTGAAGAAAGGATTTTGGCTGTTCTTCAGTGGCTGCAGCTTCCAAAAGATGAAAGACCACACT
TTTACACTTTGTATTTGGAAGAACCAGATTCTTCAGGTCATTCATATGGACCAGTCAGCAGTGAAGTCATCAAA
GCCTTGCAAGGGTTGATGGTATGGTTGGTATGCTGATGGATGGTCTGAAAGAGCTGAACTGCACAGATGC
CTGAACCTCATCCTTATTTAGATCATGGCATGGAACAAGGCAGTTGTAAGAAATACATATATCTGAATAAGTA
TTTGGGGGATGTTAAAAATATTAAGTTATCTATGGACCTGCAGCTCGATTGAGACCCTCTGATGTCCAGATA
AATACTATTCATTTAACTATGAAGGCATTGCCCCGAAATCTTTCTTGCCGGGAACCAAAACCAGCACTTCAAACCT
TATCTGAAACATTTCTTGCTAAGCGTTTGCACTTTGCTAAGAGTGATAGAATTGAGCCCTTGACATTCTATTTG
GACCCTCAGTGGCAACTTGCAATCCCTCAGAAAGGAAATATTGTGGAAGTGGATTTTCATGGCTCTGACA
ATGTGTTTTCAAATATGCAAGCCCTCTTTGTTGGCTATGGACCTGGATTCAAGCATGGCATTGAGGCTGACACC
TTTGAAGCAATTGAAGTCTATAACTTGATGTGTGATTTGCTGAATTTGACACCGGCTCCTAATAACGGAACCTCA
TGGAAGTCTTAACCACTTCTGAAGAATCCTGTTTATACGCCAAAGCATCCCAAAGAAGTGACCCCCCTGGTGC
AGTGCCCCCTTACAAGAAACCCAGAGATAACCTTGGCTGCTCATGTAACCCCTTCATTTTGCCGATTGAGGAT
TTTCAAACACAGTTCAATCTGACCGTGGCAGAAGAGAAGATTATTAAGCATGAACTTTGCCCTATGGAAGAC
CTAGAGTTCTCCAGAAGGAAAACACCATCTGTCTTCTTTCCAGCACCACTTATGAGTGGATACAGCCAAGAC
ATCTTGATGCCCCCTTTGGACATCCTATACCGTGGACAGAAATGACAGTTTCTCTACGGAAGACTTCTCCAACCTG
TCTGTACCAGGACTTTAGAATTCCTCTTAGTCCTGTCCATAAATGTTCATTTTATAAAAAATAACACCAAAGTGAG
TTACGGGTTCTCTCCCCACCACAACCTGAATAAGAATTCAAGTGGAATATATTCTGAAGCCTTGCTTACTACAA
ATATAGTGCCAATGTACCAGAGTTTTCAAGTTATATGGCGCTACTTTCATGACACCCTCTTGCGAAAGTATGCA
GAAGAAAGAAATGGTGTCAATGTCGTCAGTGGTCCTGTGTTTGACTTTGATTATGATGGACGTTGTGATTCT
TGGAGAATTTGAGGCAAAAAAGAAGAGTCATCCGTAACCAAGAAATTTGATTCCAACCTATTTCTTCATTGTG
CTGACAAGCTGTAAAGATACATCTCAGACGCCTTGCACTGTGAAAACCTGGACACCTTGCTTTTCATTTTGCC
TCACAGGACTGATAACAGCGAGAGCTGTGTGCATGGGAAGCATGACTCCTCATGGGTTGAAGAATTGTTGAT
GTTGCACAGAGCACGGATCACAGACGTCGAGCACATCACTGGACTCAGCTTTTATCAACAAAGAAAAGAGCC
AGTTTCAGACATTTTGAAGTTGAAAACACATTTGCCAACCTTTAGCCAAGAAGATTGA (SEQ ID NO:5)

Fig. 5

TAGssNPP1 (N-terminus D8; signal peptide sequence underlined and the targeting moiety in bold)

IGVLLTQRTLLSLVLALLFPSMASM**DDDDDDDD**DAGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCG
TYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPWVTAKY
QGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEEIRILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYG
PVSSEVIKALQRVDGMVGMMLMDGLKELNLHRCNLILISDHGMEQGSCCKYIYLNKYLGDVKNIKVIYGP
AARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNP
SERKYCGSGFHGSDNVFSNMQALFVGYPGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLN
HLLKNPVYTPKHPKEVHPLVQCPFTRNPRDNLGCSNPSILPIEDFQTQFNLTVAEEKIIKHETLPYGRPRV
LQKENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTK
VSYGFLSPPQLNKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHDTLRKYAEERNGVNVVSGPVFDFDYD
GRCDSENLRQKRRVIRNQEILIPTHFFIVLTSCKDTSQTPLHCENLDTLAFILPHRTDNSESCVHGKHDSS
WVEELLMLHRARITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFSQED (SEQ ID NO:6)

Fig. 6

ssNPP1 (2238bp)

ATGGGTGTA CTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCAAGCATGGCGAGCA
TGGCAGGGTTTGAAACGCCTCCTACACTCTTGTTTTCTTTGGATGGATT CAGGGCAGAATATTTGCACACTTGG
GGTGGACTTCTTCTGTTATTAGCAAAC TCAAAAAATGTGGAACATATACTAAAAACATGAGACCGGTGTATC
CAACAAAAACTTTCCCAATCACTACAGCATTGTCACCGGATTGTATCCAGAATCTCATGGCATAATCGACAAT
AAGATGTATGATCCCAAAATGAATGCTTCTTTCACTTAAAAAGTAAAGAGAAATTTAATCCGGAGTGGTACA
AAGGAGAACCAATTTGGGTACAGCTAAGTATCAAGGCCTCAAGTCTGGCACATTTTTCTGGCCAGGATCAGA
TGTGGAAATTAACGGAATTTTCCAGACATCTATAAAATGTATAATGGTTCAGTGCCATTTGAAGAAAGGATT
TGGCTGTTCTTCAGTGGCTGCAGCTTCCAAAAGATGAAAGACCACACTTTTACACTTTGTATTTGGAAGAACCA
GATTCTTCAGGTCATTCATATGGACCAGTCAGCAGTGAAGTCATCAAAGCCTTG CAGAGGGTTGATGGTATGG
TTGGTATGCTGATGGATGGTCTGAAAGAGCTGAACTTGACAGATGCCTGAACCTCATCCTTATTT CAGATCAT
GGCATGGAACAAGGCAGTTGTAAGAAATACATATATCTGAATAAGTATTTGGGGGATGTTAAAAATATTTAA
GTTATCTATGGACCTGCAGCTCGATTGAGACCCTCTGATGTCCAGATAAATACTATTCATTTAACTATGAAGG
CATTGCCCGAAATCTTTCTTGCCGGGAACCAAACCAGCACTTCAAACCTTATCTGAAACATTTCTTGCCTAAGC
GTTTGCATTTGCTAAGAGTGATAGAATTGAGCCCTTGACATTCTATTTGGACCCTCAGTGGCAACTTGCA TTG
AATCCCTCAGAAAGGAAATATTGTGGAAGTGGATTT CATGGCTCTGACAATGTGTTTTCAAATATGCAAGCCC
TCTTTGTTGGCTATGGACCTGGATTCAAGCATGGCATTGAGGCTGACACCTTTGAAAACATTGAAGTCTATAAC
TTGATGTGTGATTTGCTGAATTTGACACCGGCTCCTAATAACGGAAC TCAAGTCTTAACCACTTCTGAA
GAATCCTGTTTATACGCCAAAGCATCCCAAAGAAGTGCACCCCCTGGTGCAGTGCCCCTTCACAAGAAACCCC
AGAGATAACCTTGGCTGCTCATGTAACCCTTCCATTTTGCCGATTGAGGATTTTCAAACACAGTTCAATCTGAC
CGTGGCAGAAGAGAAGATTATTAAGCATGAAACTTTGCCCTATGGAAGACCTAGAGTTCTCCAGAAGGAAAA
CACCATCTGTCTTTTCCAGCACCAGTTTATGAGTGGATACAGCCAAGACATCTTGATGCCCCTTTGGACATC
CTATACCGTGGACAGAAATGACAGTTTCTCTACGGAAGACTTCTCCA ACTGTCTGTACCAGGACTTTAGAATTC
CTCTTAGTCCTGTCCATAAATGTTCATTTTATAAAAAATAACCCAAAGTGAGTTACGGGTTCTCTCCCCACCAC
AACTGAATAAGAATTCAAGTGGAAATATATTCTGAAGCCTTGCTTACTACAAATATAGTGCCAATGTACCAGAG
TTTTCAAGTTATATGGCGCTACTTT CATGACACCCTCTTGCGAAAGTATGCAGAAGAAAGAAATGGTGTCAAT
GTCGTCAGTGGTCCTGTGTTTGACTTTGATTATGATGGACGTTGTGATTCC TTGGAGAATTTGAGGCAAAAAA
GAAGAGTCATCCGTAACCAAGAAATTTTGATTCCAAC TCAATTTCTTATTGTGCTGACAAGCTGTAAAGATACA
TCTCAGACGCCTTTGCACTGTGAAAACCTGGACACCTTGCTTTCA TTTTGCTCACAGGACTGATAACAGCGA
GAGCTGTGTGCATGGGAAGCATGACTCCTCATGGGTTGAAGAATTGTTGATGTTGCACAGAGCACGGATCAC
AGACGTCGAGCATCACTGGACTCAGCTTTTATCAACAAAGAAAAGAGCCAGTTTCAGACATTTTGAAGTTG
AAAACACATTTGCCAACCTTTAGCCAAGAAGAT (SEQ ID NO:7)

Fig. 7

ssNPP1 (signal peptide sequence underlined)

IGVLLTQRTLLSLVLALLFPSMASMAGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCGTYTKNMRPV
YPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPiWVTAKYQGLKSGTFF
WPGSDVEINGIFPDIYKMYNGSVPFEEILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKAL
QRVDGMVGMMLMDGLKELNLHRCLNLILISDHGMEQGSCKKIYILNKYLGDVKNIKVIYGPAARLRPSDV
PDKYYSFNYEGiARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKCYCGSG
FHGSDNVFSNMQALFVGYPGPGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLLKNPVYTP
KHPKEVHPLVQCPFTRNPRDNLGCSCNPSILPIEDFQTQFNLTVAEEKIIKHETLPYGRPRVLQKENTICLLS
QHQMMSGYSQDILMPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQL
NKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHDTLLRKYAEERNGVNVVSGPVFDFDYDGRCDSENLRQ
KRRVIRNQEILIPTHFFIVLTSCKDTSQTPLHCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRA
RITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFSQED (SEQ ID NO:8)

Fig. 8

sNPP1

ATGGGTGTACTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCAAGCATGGCGAGCA
TGCCAAGTTGTGCCAAAGAAGTTAAAAGTTGCAAAGGTCGCTGTTTCGAGAGAACATTTGGGAACTGTCGCT
GTGATGCTGCCTGTGTTGAGCTTGGAAACTGCTGTTTGGATTACCAGGAGACGTGCATAGAACCAGAACATAT
ATGGACTTGCAACAAATTCAGGTGTGGTGAGAAAAGATTGACCAGAAGCCTCTGTGCCTGTTTCAGATGATTGC
AAGGACAAGGGCGACTGCTGCATCAACTACAGTTCAGTGTGTCAAGGTGAGAAAAGTTGGGTGGAAGAACC
ATGTGAGAGCATTAAATGAGCCACAGTGCCAGCAGGGTTTGAAACGCCTCCTACACTCTTGTTTTCTTTGGATG
GATTCAGGGCAGAATATTTGCACACTTGGGGTGGACTTCTTCCTGTTATTAGCAAACCTCAAAAAATGTGGAAC
ATATACTAAAAACATGAGACCGGTGTATCCAACAAAACTTTCCCAATCACTACAGCATTGTCACCGGATTGT
ATCCAGAATCTCATGGCATAATCGACAATAAGATGTATGATCCAAAATGAATGCTTCCTTTTCACTTAAAAGT
AAAGAGAAATTTAATCCGGAGTGGTACAAAGGAGAACCAATTTGGGTCACAGCTAAGTATCAAGGCCTCAAG
TCTGGCACATTTTTCTGGCCAGGATCAGATGTGGAAATTAACGGAATTTCCAGACATCTATAAAATGTATAA
TGGTTCAGTGCCATTTGAAGAAAGGATTTTGGCTGTTCTTCAGTGGCTGCAGCTTCCAAAAGATGAAAGACCA
CACTTTTACACTTTGTATTTGGAAGAACCAGATTCTTCAGGTCATTATATGGACCAGTCAGCAGTGAAGTCAT
CAAAGCCTTGCAAGGGTGTATGGTATGGTGTGATGCTGATGGATGGTCTGAAAGAGCTGAACCTGCACAG
ATGCCTGAACCTCATCCTTATTTAGATCATGGCATGGAACAAGGCAGTTGTAAGAAATACATATATCTGAATA
AGTATTTGGGGGATGTTAAAAATATTAAGTTATCTATGGACCTGCAGCTCGATTGAGACCCTCTGATGTCCTCA
GATAAATACTATTCATTTAACTATGAAGGCATTGCCCCGAAATCTTTCTTGCCGGGAACCAAACCAGCACTTCAA
ACCTTATCTGAAACATTTCTTGCTAAGCGTTTGCACTTTGCTAAGAGTGATAGAATTGAGCCCTTGACATTCTA
TTTGGACCCTCAGTGGCAACTTGCATTGAATCCCTCAGAAAGGAAATATTGTGGAAGTGGATTTTCATGGCTCT
GACAATGTGTTTTCAAATATGCAAGCCCTCTTTGTTGGCTATGGACCTGGATTCAAGCATGGCATTGAGGCTG
ACACCTTTGAAAACATTGAAGTCTATAACTTGATGTGTGATTGCTGAATTTGACACCGGCTCCTAATAACGGA
ACTCATGGAAGTCTTAACCACTTCTGAAGAATCCTGTTTATACGCCAAAGCATCCCAAAGAAGTGCACCCCT
GGTGCAGTGCCCTTCACAAGAAACCCAGAGATAACCTTGCTGCTCATGTAACCTTCCATTTTGCCGATTG
AGGATTTTCAAACACAGTTCAATCTGACCGTGGCAGAAGAGAAGATTATTAAGCATGAAACTTTGCCCTATGG
AAGACCTAGAGTTCTCCAGAAGGAAAACACCATCTGTCTTCTTTCCAGCACCAGTTTATGAGTGGATACAGCC
AAGACATCTTGATGCCCCCTTGGACATCCTATACCGTGGACAGAAATGACAGTTTCTCTACGGAAGACTTCTCC
AACTGTCTGTACCAGGACTTTAGAATTCCTCTTAGTCCTGTCCATAAATGTTCATTTTATAAAAATAACACCAA
GTGAGTTACGGGTTCCTCTCCCCACCACAACCTGAATAAGAATTCAAGTGAATATATTCTGAAGCCTTGCTTAC
TACAAATATAGTGCCAATGTACCAGAGTTTTCAAGTTATATGGCGCTACTTTCATGACACCCTCTTGCGAAAGT
ATGCAGAAGAAAGAAATGGTGTCAATGTGTCAGTGGTCCTGTGTTTGACTTTGATTATGATGGACGTTGTGA
TTCCTTGGAGAATTTGAGGCCAAAAAGAAGAGTCATCCGTAACCAAGAAATTTTGATTCCAACCTCATTTCTTCA
TTGTGCTGACAAGCTGTAAAGATACATCTCAGACGCCTTTGCACTGTGAAAACCTGGACACCTTGGCTTTCATT
TTGCCTCACAGGACTGATAACAGCGAGAGCTGTGTGCATGGGAAGCATGACTCCTCATGGGTTGAAGAATTG
TTGATGTTGCACAGAGCACGGATCACAGACGTCGAGCACATCACTGGACTCAGCTTTTATCAACAAAGAAAAG
AGCCAGTTTCAGACATTTTGAAGTTGAAAACACATTTGCCAACCTTTAGCCAAGAAGAT (SEQ ID NO:9)

Fig. 9

sNPP1

IGVLLTQRTLLSVLALLFPSMASMPSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPE
HIWTCNKFRCGEKRLTRSLCACSDDCCKDKGDCCINYSSVCQGEKSWVEEPCESINEPQCPAGFETPPTLLF
SLDGFRAEYLHTWGGLLPVISKLLKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMN
ASFSLKSKEKFNPEWYKGEPWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEEERILAVLQ
WLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMLMDGLKELNLHRCLNLILISDHG
MEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFKPYLKHFLPK
RLHFAKSDRIEPLTFYLDPQWQLALNPSEKYGSGFGSDNVFSNMQALFVGYGPGFKHGIEADTFENI
EVYNLMCDLLNLTPAPNNGTHGSLNHLLKNPVYTPKHPKEVHPLVQCPFTRNPRDNLGCSCNPSILPIED
FQTQFNLTVAEEKIIKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTEDF
SNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHDTL
LRKYAEERNGVNVVSGPVDFDYDGRCDLENLRQKRRVIRNQEILIPTHFFIVLTSCKDTSQTPLHCENLD
TLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFSQE
D (SEQ ID NO:10)

Fig. 10

TAGsNPP1 (N-terminus D8)

ATGGGTGTA CTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCAAGCATGGCGAGCA
TGGATGACGATGATGACGACGATGACCCAAGTTGTGCCAAAGAAGTTAAAAGTTGCAAAGGTCGCTGTTTCG
AGAGAACATTTGGGAAGTGTGCTGTGATGCTGCCTGTGTTGAGCTTGGAAGTCTGTTTGGATTACCAGGA
GACGTGCATAGAACCAGAACATATATGGACTTGCAACAAATTCAGGTGTGGTGAGAAAAGATTGACCAGAAG
CCTCTGTGCCTGTTTCTGATGATTGCAAGGACAAGGGCGACTGCTGCATCAACTACAGTTCAGTGTGTCAAGGT
GAGAAAAGTTGGGTGGAAGAACCATGTGAGAGCATTAAATGAGCCACAGTGCCCAGCAGGGTTTGAAACGCC
TCCTACACTCTGTTTTCTTTGGATGGATTGAGGGCAGAATATTTGCACACTTGGGGTGGACTTCTTCTCTGTTAT
TAGCAAACTCAAAAAATGTGGAACATATACTAAAAACATGAGACCGGTGTATCCAACAAAACTTTCCCAAT
CACTACAGCATTGTCAACGGATTGTATCCAGAATCTCATGGCATAATCGACAATAAGATGTATGATCCCAAAAT
GAATGCTTCTTTTTCACTTAAAAGTAAAGAGAAAATTAATCCGGAGTGGTACAAAGGAGAACCAATTTGGGTC
ACAGCTAAGTATCAAGGCCTCAAGTCTGGCACATTTTTCTGGCCAGGATCAGATGTGGAAATTAACGGAATTT
TCCCAGACATCTATAAAATGTATAATGGTTCAGTGCCATTTGAAGAAAGGATTTTGGCTGTTCTTCAGTGGCTG
CAGCTTCCAAAGATGAAAGACCACACTTTTACACTTTGTATTTGGAAGAACCAGATTCTTCAGGTCATTCTATA
TGGACCAGTCAGCAGTGAAGTCATCAAAGCCTTGACAGAGGGTTGATGGTATGGTTGGTATGCTGATGGATGG
TCTGAAAGAGCTGAACTTGACAGATGCCTGAACCTCATCCTTATTTAGATCATGGCATGGAACAAGGCAGT
TGTAAGAAATACATATATCTGAATAAGTATTTGGGGGATGTTAAAAATATTAAAGTTATCTATGGACCTGCAG
CTCGATTGAGACCTCTGATGTCCAGATAAAATACTATTCATTTAACTATGAAGGCATTGCCCGAAATCTTTCTT
GCCGGGAACCAACCAGCACTTCAAACCTTATCTGAAACATTTCTTGCCTAAGCGTTTGCACTTTGCTAAGAGT
GATAGAATTGAGCCCTTGACATTCTATTTGGACCCTCAGTGGCAACTTGCAATTGAATCCCTCAGAAAGGAAAT
ATTGTGGAAGTGGATTTCTATGGCTCTGACAATGTGTTTTCAAATATGCAAGCCCTCTTTGTTGGCTATGGACCT
GGATTCAAGCATGGCATTGAGGCTGACACCTTTGAAAACATTGAAGTCTATAACTTGATGTGTGATTTGCTGA
ATTTGACACCGGCTCCTAATAACGGAACTCATGGAAGTCTTAACACCTTCTGAAGAATCCTGTTTATACGCCA
AAGCATCCCAAGAAGTGCACCCCTGGTGCAGTGCCCTTCACAAGAAACCCAGAGATAACCTTGGCTGCT
CATGTAACCTTCCATTTTGCCGATTGAGGATTTTCAAACACAGTTCAATCTGACCGTGGCAGAAGAGAAGATT
ATTAAGCATGAACTTTGCCCTATGGAAGACCTAGAGTTCTCCAGAAGGAAAACACCATCTGTCTTCTTTCCCA
GCACCAGTTTATGAGTGGATACAGCCAAGACATCTTGATGCCCCTTTGGACATCCTATACCGTGGACAGAAAT
GACAGTTTCTCTACGGAAGACTTCTCCAACCTGTCTGTACCAGGACTTTAGAATTCCTCTTAGTCCTGTCCATAAA
TGTTCATTTTATAAAAATAACACCAAAGTGAGTTACGGGTTCTCTCCCCACCACAACTGAATAAGAATTCAAG
TGGAATATATTCTGAAGCCTTGCTTACTACAAATATAGTGCCAATGTACCAGAGTTTTCAAGTTATATGGCGCT
ACTTTCATGACACCTCTTGCGAAAGTATGCAGAAGAAAGAAATGGTGTCAATGTCGTCAAGTGGTCCTGTGTT
TGACTTTGATTATGATGGACGTTGTGATTCTTGGAGAATTTGAGGCCAAAAAGAGATCATCCGTAACCAA
GAAATTTTGATTCCAACCTCATTTCTTCATTGTGCTGACAAGCTGTAAAGATACATCTCAGACGCCTTTGCACTGT
GAAAACCTGGACACCTTGGCTTTCATTTTGCCTCACAGGACTGATAACAGCGAGAGCTGTGTGCATGGGAAGC
ATGACTCCTCATGGGTTGAAGAATTGTTGATGTTGCACAGAGCACGGATCACAGACGTCGAGCACATCACTGG
ACTCAGCTTTTATCAACAAAGAAAAGAGCCAGTTTCAGACATTTTGAAGTTGAAAACACATTTGCCAACCTTTA
GCCAAGAAGAT (SEQ ID NO:11)

Fig. 11

TAGsNPP1 (N-terminus D8)

IGVLLTQRTLLSLVLALLFPSMASM**DDDDDDDD**PSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCL
DYQETCIEPEHIWTCNKFRGCEKRLTRSLCACSDDCCKDKGDCCINYSSVCQGEKSWVEEPCESINEPQCP
AGFETPPTLLFSLDGFRAEYLHTWGGLLPVISKLKKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIID
NKMYDPKMNASFSLKSKEKFNPEWYKGEPWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSV
PFEERILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLH
RCLNLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQ
HFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKCYGSGFHGSDNVFSNMQALFVGYPGPF
KHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLLKNPVYTPKHPKEVHPLVQCPFTRNPRDNL
GCSCNPSILPIEDFQTQFNLTVAEEKIHKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDILMPLWTSYT
VDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEALLTTNIVPMYQS
FQVIWRYFHDTLRLKYAEERNGVNVVSGPVDFDYDGRCDLENLRQKRRVIRNQEILIPTHFFIVLTSCK
DTSQTPHLCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDVEHITGLSFYQQRKEPVSD
ILKLKTHLPTFSQED (SEQ ID NO:12)

Fig. 12

TAGsNPP1 (C-terminus D8)

GTGGGTGTACTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCAAGCATGGCGAGCA
TGCCAAGTTGTGCCAAAGAAGTTAAAAGTTGCAAAGGTCGCTGTTTCGAGAGAACATTTGGGAACTGTCGCT
GTGATGCTGCCTGTGTTGAGCTTGAAACTGCTGTTTGGATTACCAGGAGACGTGCATAGAACCAGAACATAT
ATGGACTTGCAACAAATTCAGGTGTGGTGAGAAAAGATTGACCAGAAGCCTCTGTGCCTGTTGAGATGATTGC
AAGGACAAGGGCGACTGCTGCATCAACTACAGTTCAAGGTGAGAAAAGTTGGGTGGAAGAACC
ATGTGAGAGCATTAAATGAGCCACAGTGCCAGCAGGGTTTGAAACGCCTCCTACACTCTGTTTTCTTTGGATG
GATTCAGGGCAGAATATTTGCACACTTGGGGTGGACTTCTTCTGTTATTAGCAAACCTCAAAAAATGTGGAAC
ATATACTAAAAACATGAGACCGGTGTATCCAACAAAACTTTCCCAATCACTACAGCATTGTCACCGGATTGT
ATCCAGAATCTCATGGCATAATCGACAATAAGATGTATGATCCCAAATGAATGCTTCCTTTTCACTTAAAAGT
AAAGAGAAATTTAATCCGGAGTGGTACAAAGGAGAACCAATTTGGGTACAGCTAAGTATCAAGGCCTCAAG
TCTGGCACATTTTTCTGGCCAGGATCAGATGTGGAATTAACGGAATTTCCAGACATCTATAAAATGTATAA
TGTTTCAGTGCCATTTGAAGAAAGGATTTGGCTGTTCTTCAGTGGCTGCAGCTTCCAAAGATGAAAGACCA
CACTTTTACACTTTGTATTTGGAAGAACCAGATTCTTCAGGTCATTATATGGACCAGTCAGCAGTGAAGTCAT
CAAAGCCTTGACAGAGGGTTGATGGTATGGTTGGTATGCTGATGGATGGTCTGAAAGAGCTGAACTTGACAG
ATGCCTGAACCTCATCCTTATTTAGATCATGGCATGGAACAAGGCAGTTGTAAGAAATACATATATCTGAATA
AGTATTTGGGGGATGTTAAAAATATTAAGTTATCTATGGACCTGCAGCTCGATTGAGACCCTCTGATGTCCCA
GATAAATACTATTCATTTAACTATGAAGGCATTGCCCGAAATCTTCTTGCCGGAACCAAACCAGCACTTCAA
ACCTTATCTGAAACATTTCTTGCCTAAGCGTTTGCACCTTGCTAAGAGTGATAGAATTGAGCCCTTGACATTCTA
TTTGACCCCTCAGTGGCAACTTGCAATTGAATCCCTCAGAAAGGAAATATTGTGGAAGTGGATTTTATGGCTCT
GACAATGTGTTTTCAAATATGCAAGCCCTCTTTGTTGGCTATGGACCTGGATTCAAGCATGGCATTGAGGCTG
ACACCTTTGAAAACATTGAAGTCTATAACTTGATGTGTGATTGCTGAATTTGACACCGGCTCCTAATAACGGA
ACTCATGGAAGTCTTAACCACTTCTGAAGAATCCTGTTTATACGCCAAAGCATCCCAAAGAAGTGCACCCCT
GGTGCAGTGCCCTTCACAAGAAACCCAGAGATAACCTTGGCTGCTCATGTAACCTTCCATTTTGCCGATTG
AGGATTTTCAAACACAGTTCAATCTGACCGTGGCAGAAGAGAAGATTATTAAGCATGAACTTTGCCCTATGG
AAGACCTAGAGTTCTCCAGAAGGAAAACACCATCTGTCTTCTTTCCAGCACCAGTTTATGAGTGGATACAGCC
AAGACATCTTGATGCCCCCTTTGGACATCCTATACCGTGGACAGAAATGACAGTTTCTCTACGGAAGACTTCTCC
AACTGTCTGTACCAGGACTTTAGAATTCCTCTTAGTCCTGTCCATAAATGTTCAATTTATAAAAAATAACACCAAA
GTGAGTTACGGGTTTCTCTCCCCACCACAACCTGAATAAGAATTCAAGTGGAATATATTCTGAAGCCTTGCTTAC
TACAAATATAGTGCCAATGTACCAGAGTTTTCAAGTTATATGGCGCTACTTTCATGACACCCTCTGCGAAAGT
ATGCAGAAGAAAGAAATGGTGTCAATGTCGTCAGTGGTCCTGTGTTTACTTTGATTATGATGGACGTTGTGA
TTCCTTGGAGAATTTGAGGCAAAAAGAAGAGTCATCCGTAACCAAGAAATTTTGATTCCAACCTCATTTCTTCA
TTGTGCTGACAAGCTGTAAAGATACATCTCAGACGCCTTTGCACTGTGAAAACCTGGACACCTTGGCTTTCAAT
TTGCCTCACAGGACTGATAACAGCGAGAGCTGTGTGCATGGGAAGCATGACTCCTCATGGGTGGAAGAATTG
TTGATGTTGCACAGAGCACGGATCACAGACGTCGAGCACATCACTGGACTCAGCTTTTATCAACAAAGAAAAG
AGCCAGTTTCAGACATTTTGAAGTTGAAAACACATTTGCCAACCTTTAGCCAAGAAGATGATGACGATGATGA
CGACGATTGA (SEQ ID NO:13)

Fig. 13

TAGsNPP1 (C-terminus D8; signal peptide sequence underlined and the targeting moiety in bold)

QGVLLTQRTLLSLVLALLFPSMASMPSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPEHIWTCN
KFRCGEKRLTRSLCACSDDCCKDKGDCCINYSSVCQGEKSWVEEPCESINEPQCPAGFETPPTLLFSLDGFRAEYLHT
WGGLLPVISKLLKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKG
EPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDYKMYNGSVPFEEERILAVLQWLQLPKDERPHFYTLYLEEPDSSGH
SYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLHRCNLILISDHGMEQGSCCKYIYLNKYLGDVKNIKVIYGPAARL
RPSDVDPKYYSFNYEGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKCYGSGFH
GSDNVFSNMQALFVGYPGFGKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSLNHLLKNPVYTPKHPKEVHP
LVQCPFTRNPRDNLGCSCNPSILPIEDFQTQFNLTVAEEKIIKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDIL
MPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSGIYSEALLTTNIVPMY
QSFQVIWRYFHDTLRLKYAERNGVNVVSGPVFDFDYDGRCDLENLRQKRRVIRNQEILIPTHFFIVLTSCKDTST
PLHCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELMLHRARITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFS
QEDDDDDDDDD (SEQ ID NO:14)

Fig. 14

Linker peptide

GGGGSGGGGS (SEQ ID NO:15)

Fig. 15

The amino acid sequence of the Fc region

EPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS
DGSFFLYS KLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:16)

Fig. 16

The amino acid sequence of TAGsssNPP1 (N-terminus D8) + Fc + Linker

IGVLLTQRTLSLVLALLFPSMASMEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS
DGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK **DDDDDDDD**
GGGGSGGGGSAGFETPPTLLFSLDGFRAEYLHTWGGLLPVISLKKCGTYTKNMRPVYPTKTFPNHYSIVT
GLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPWVTAKYQGLKSGTFFWPGSDVEINGIFPDI
YKMYNGSVPFEERILAVLQWLQLPKDERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMLMD
GLKELNLHRCLNLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNL
SCREPNQHFQPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKCYCGSGFHGSDNVFSNMQALF
VGYGPGFKHGIEADTFENIEVYNLMCDLLNLTPAPNNGTHGSL (SEQ ID NO:17)

Fig. 17

The amino acid sequence of TAGsssNPP1 (C-terminus D8) + Fc + Linker

IGVLLTQRTLLSVLALLFPSMASMEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSD
GSFFLYSKLTVDKSRWQQGNVFSVMHEALHNHYTQKSLSLSPGKAGFETPPTLLFSLDGFRAEYLHTW
GGLLPVISKLKKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIIDNKMYDPKMNASFSLKSKEKFNPE
WYKGEPWVTAKYQGLKSGTFFWPGSDVEINGIFPDYKMYNGSVPFEERILAVLQWLQLPKDERPHFYT
LYLEEDSSGHSYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLRCLNLIISDHGMEQGSCKKYIYLNKY
LGDVKNIKVIYGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFQPYLKHFPLPKRLHFAKSDRIEPLTFYL
DPQWQLALNPSEKCYGSGFHGSDNVFSNMQALFVGYPGFGKHGIEADTFENIEVYNLMCDLLNLTAP
NNGTHGSLGGGGSGGGGS **DDDDDDDD** (SEQ ID NO: 18)

Fig. 18

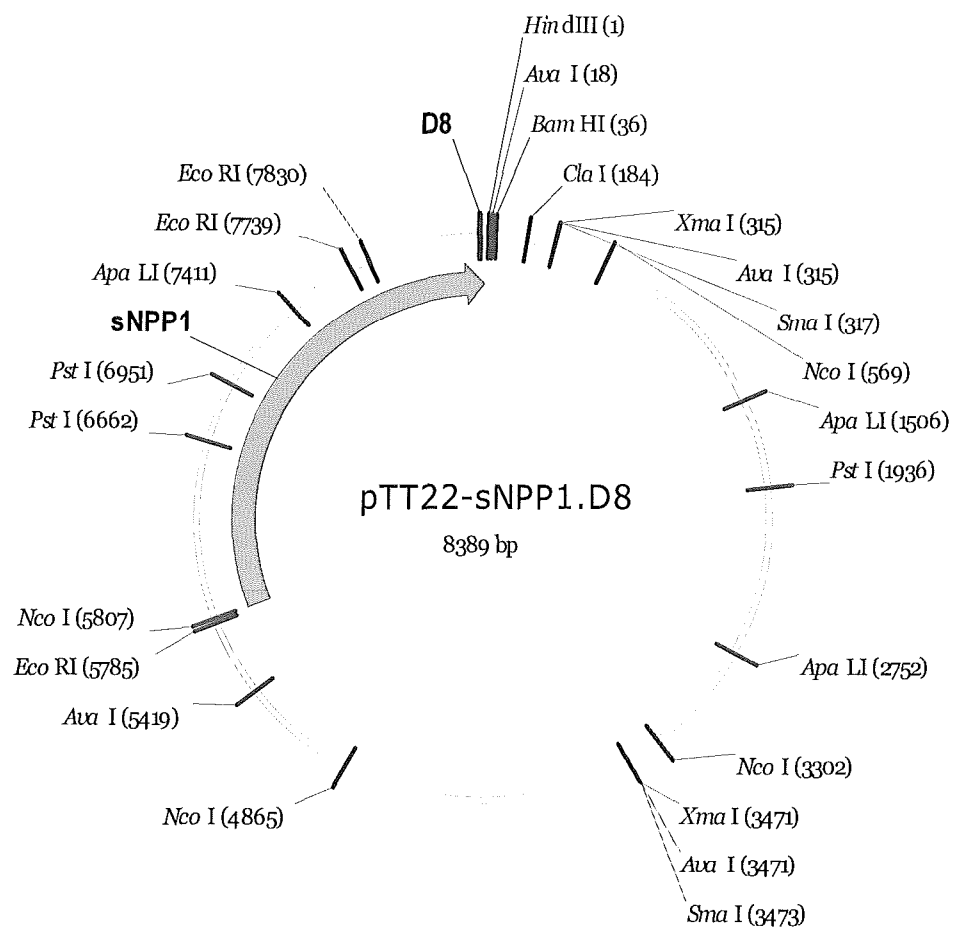


Fig. 19

Western Analysis

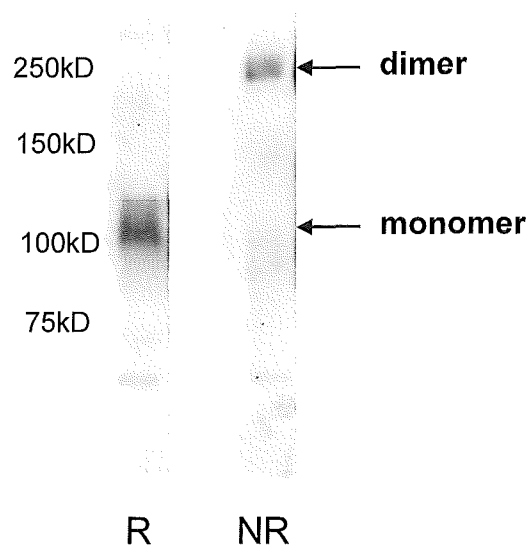


Fig. 20

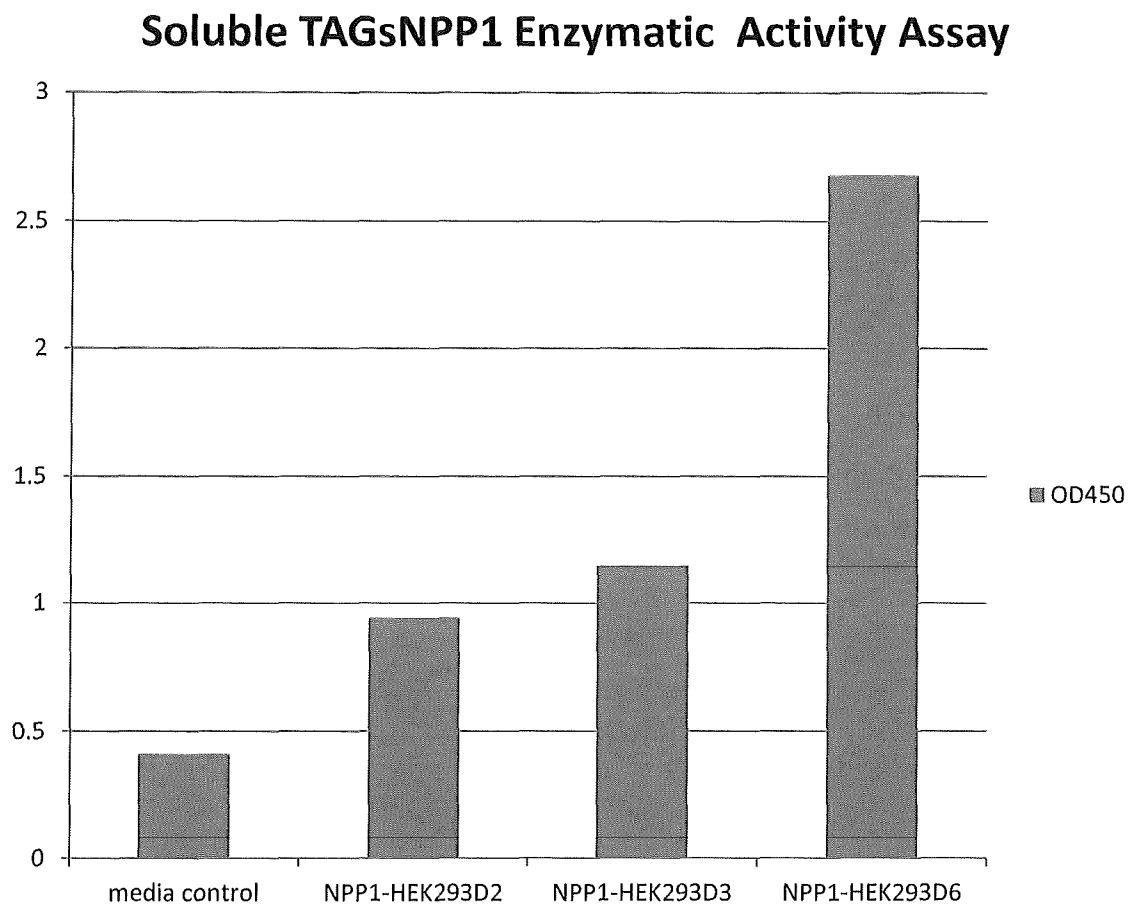


Fig. 21

Recombinant NPP1 fusion proteins

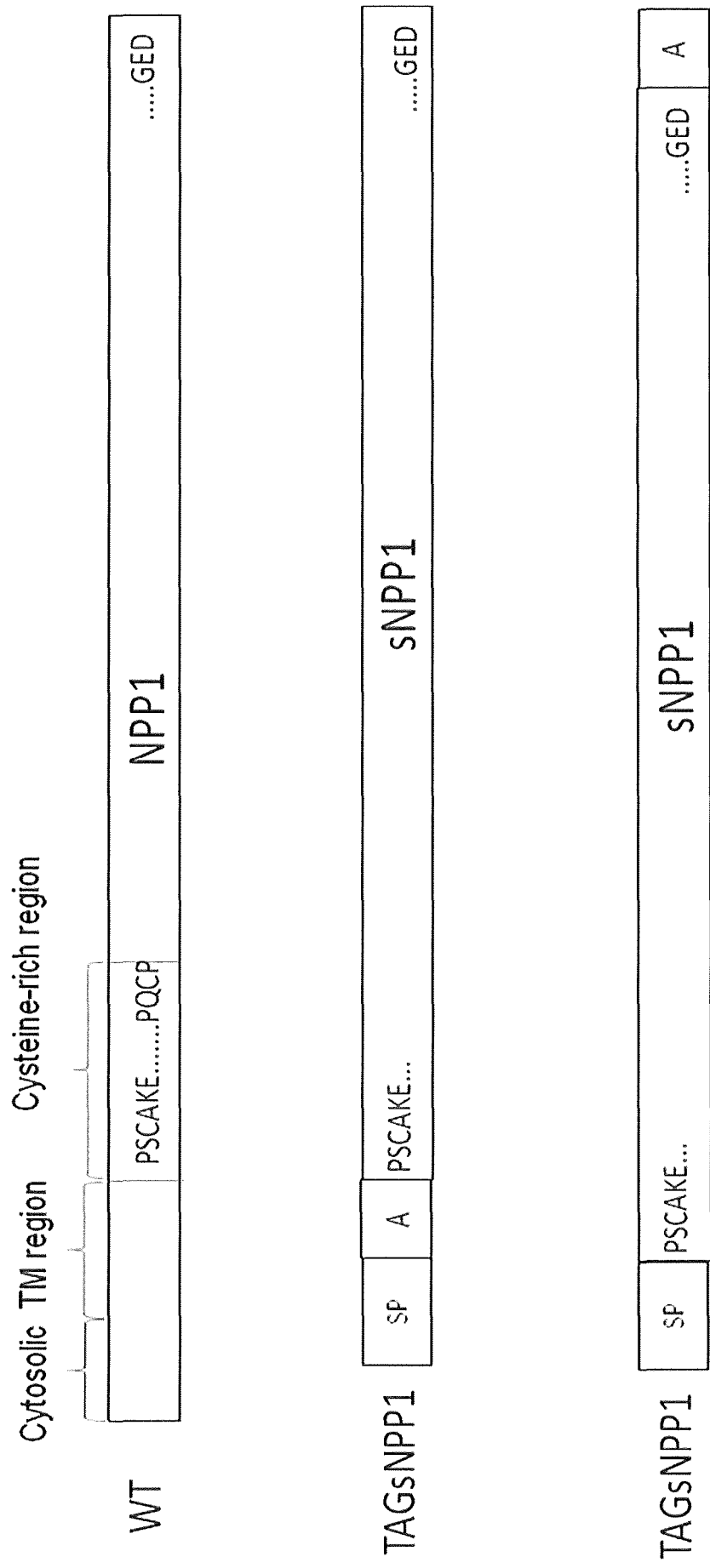


Fig. 22A

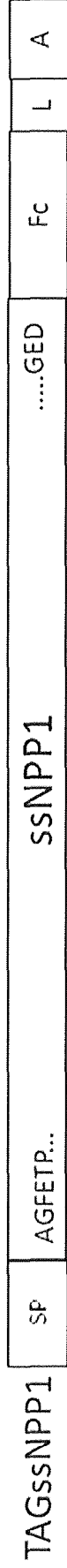
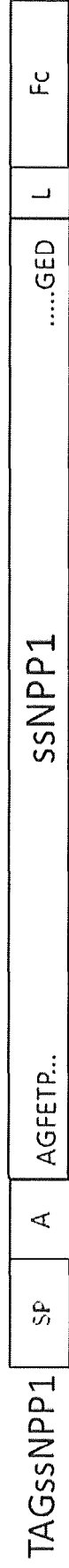


Fig. 22B

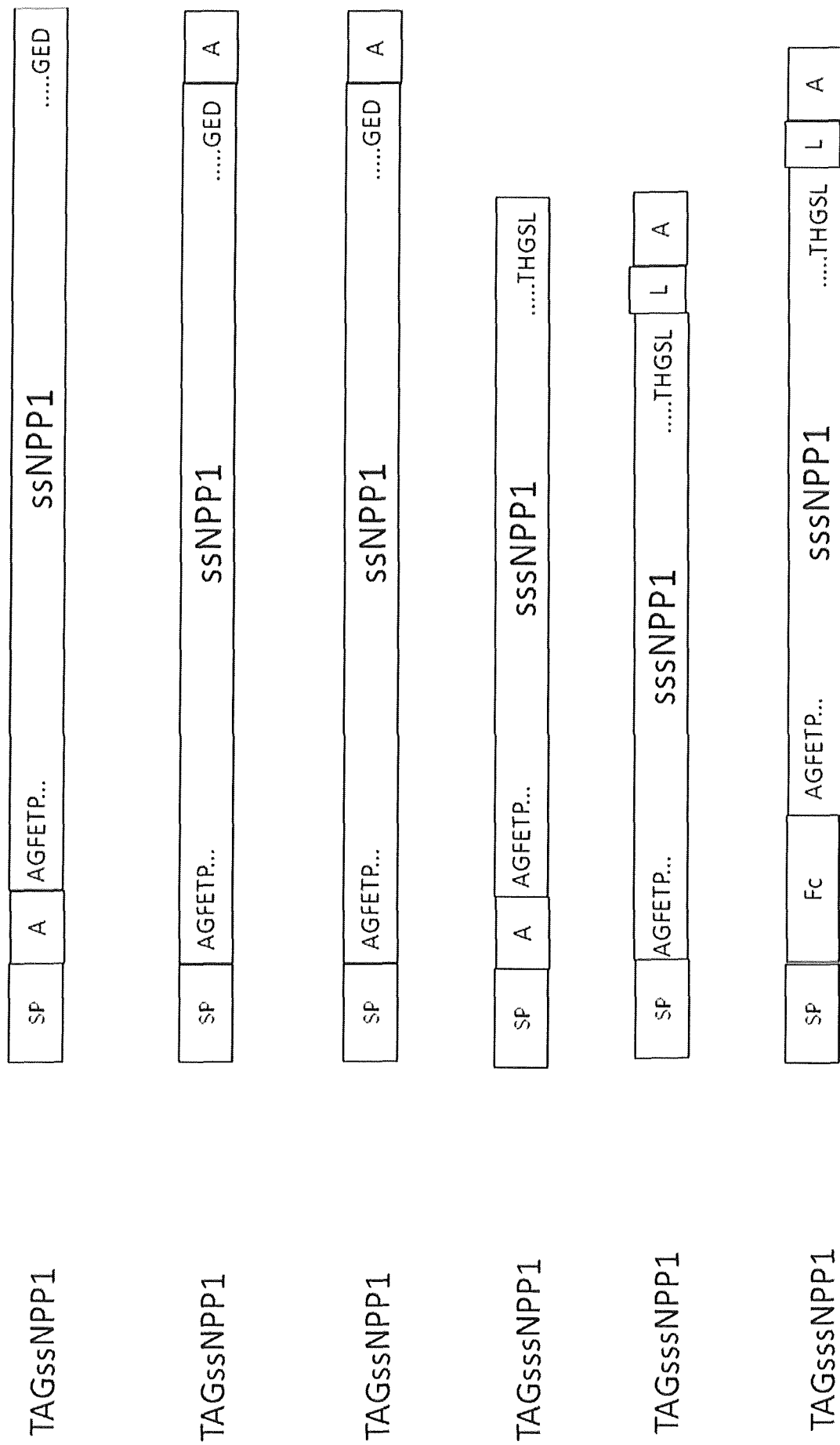


Fig. 22C

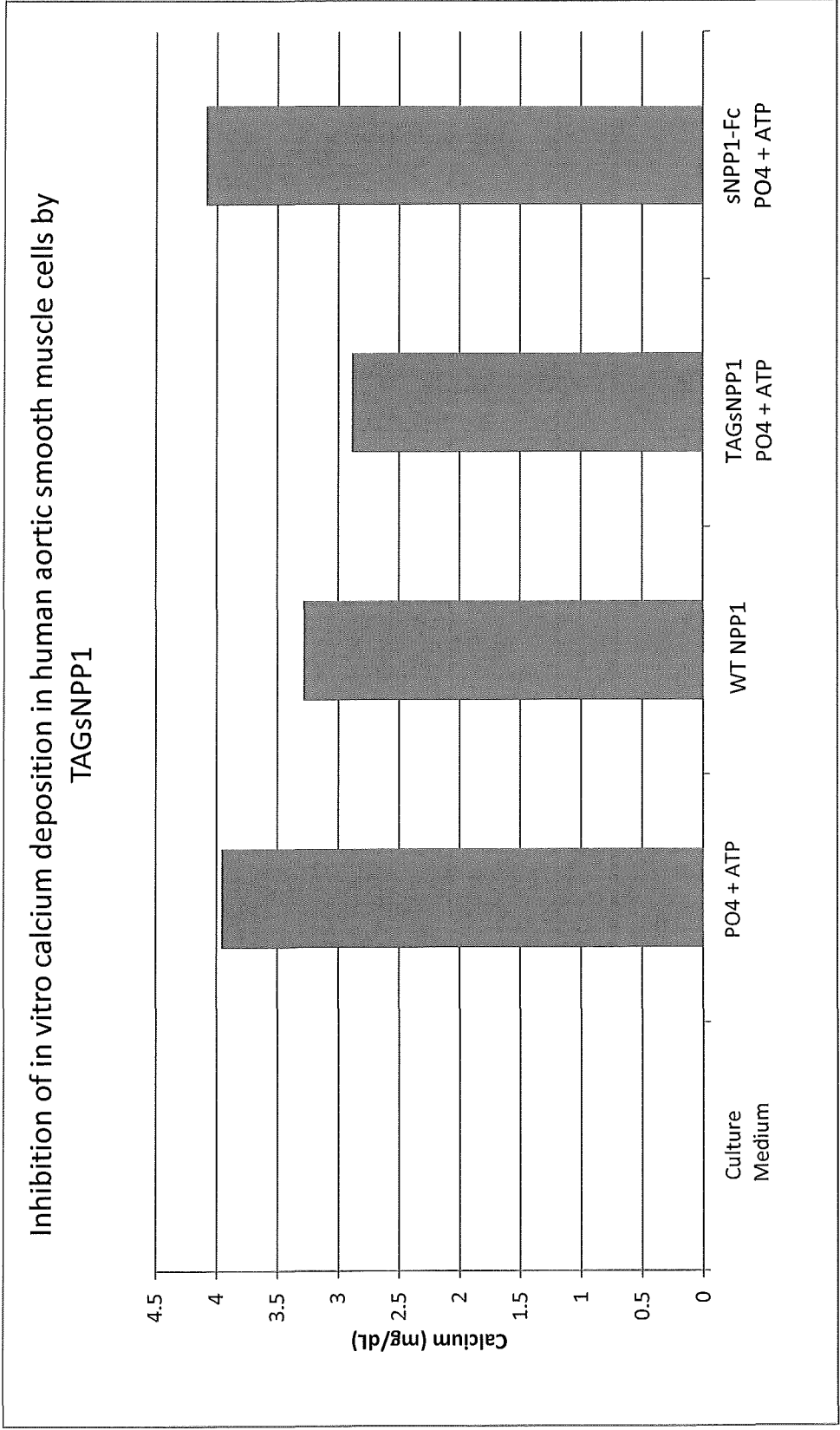


Fig. 23

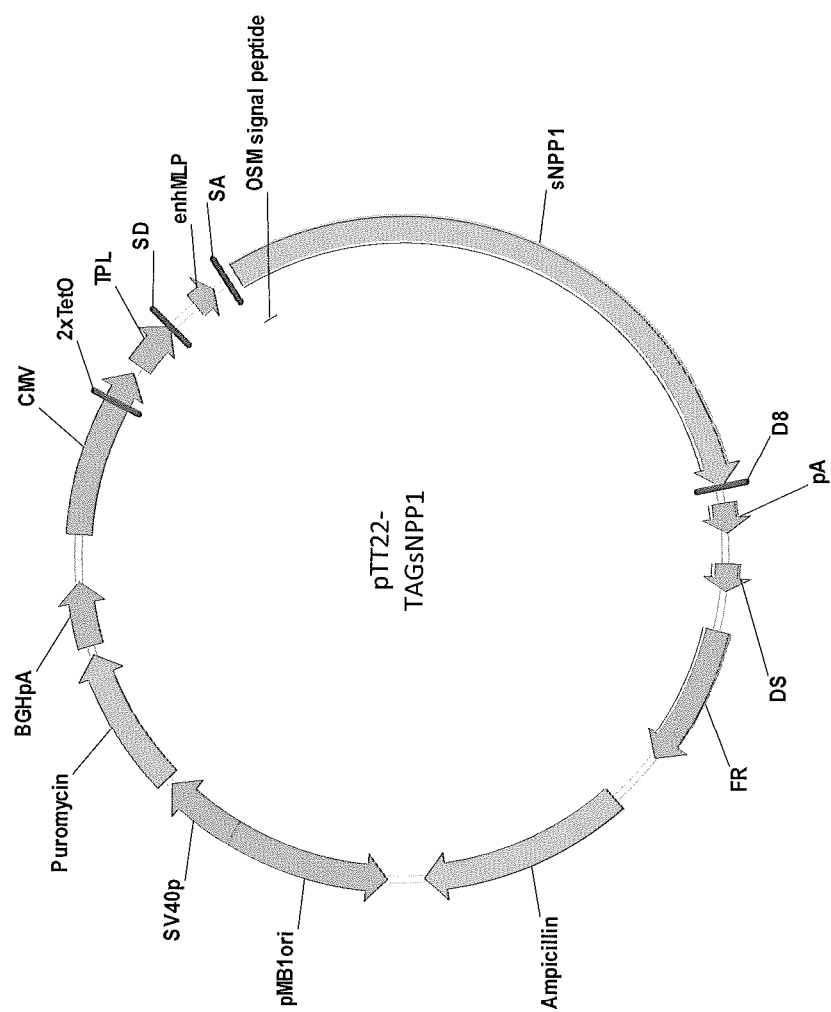


Fig. 24

DNA sequence of TAGSNPP1 (D8)

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gagacgtgcatagaaccagaaacatatatggacttgcaacaaattcaggtgtgtgagaaaaagattgaccagaagcctctgtgcctgttcagatgat
tgcaggacaaggcgactgctgcatcaactacagttcagtggtcaaggtgagaaaaagttgggtggaagaaacctgtgagagcattaatgagcca
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aacggaaattttccagacatctataaaatgtataatgggtcagtgccatttgaagaaaggattttggctgttttcagtggtgcagcttccaaaa
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gactcctcatgggtgaagaattgtgatgtgcacagagcacggatcacagacgtcgagcacatcactggactcagcttttatcaacaaagaaaa
gagccagtttcagacattttgaaagttgaaaacacacatttgccaaacctttagccaagaagatgatgacgatgacgacgattga

(SEQ ID NO: 19)

Fig. 25

Amino Acid sequence of TAGsNPP1(D8)

MGVLLTQRTLLSLVLALLFPSMASMPSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPEHIWTCNKFRCGEKRLTRSLCACSDDC
CKDKGDCCINYSVVCQGEKSWVEEPCESINEPQCPAGFETPPTLLFSLDGFRAEYLHTWGGLLPVISLKKCGTYTKNMRPVYPTKTFPNHYSIVT
GLYPESHGII DNKMYDPKMNASFSLKSKKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEEERILAVLQWLQLPK
DERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMDGLKELNLHRCNLNLISDHGMEQGSCKKYIYLNKYLGDVKNIKVIYGPAARL
RPSDVDPKYYSFNYEGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKCYCGSGFHGSDNVFSNMQALFVGYP
GFKHGIEADTFENIEVYNLMCDLLNLTAPNNGTHGSLNHLKKNPVYTPKHPKEVHPLVQCPFTRNPRDNLGCSCNPSILPIEDFQTQFNLTVAEE
KIIKHETLPYGRPRVLQKENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQL
NKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHDTLIRKYAEERNGVNVSGPVDFDYDGRCDLENLRQKRRVIRNQEILIPTHFFVLTSCKDT
SQTPLHCENLDTLAFILPHRTDNSESCVHGKHDSSWVEELLMLHRARITDVEHITGLSFYQQRKEPVSDILKLKTHLPTFSQEDDDDDDDDD

(SEQ ID NO: 20)

Fig. 26

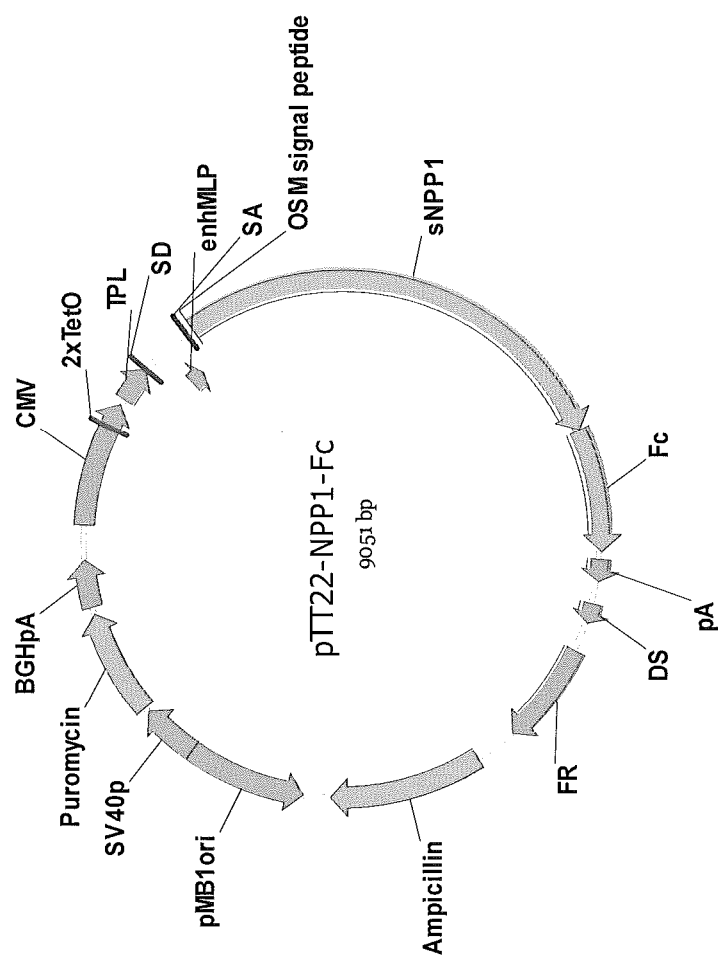


Fig. 27

ATGGGTGTA CTGCTCACAGAGGACGTGCTCAGTCTGGTCTTGCACTCCTGTTTCCAAGCATGGCGAGCATGCCAAGTTGTGCCAAAGAA GTTAAAAGTTGCCAAGGTGCGTGTTTCGAGA
GAACATTTGGGAACTGTGCTGTGATGCTGCCTGTGTTGAGCTTGGAACTGCTGTTGGATTACCGAGAGACGTGCATAGAACCAAGAACATATATGGACTTGCACAAATTCAGGTGTGGTGA
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GCATTAATGAGCCACAGTCCCGAGCAGGTTTGAAACGCTCTACACTCTGTTTCTTTGGATGGATTGAGGCGAGAAATATTTGCACACTTGGGTGGACTTCTTCTGTTATTAGCAAACTCA
AAAAATGTGGAAACATATCTAAAAACATGAGACCGGTGTATCCAAACAAAACTTTCCCAATCACTACAGCATGTGCACCGGATTGTATCCAGAAATCTCATGGCATATATCGACAATAAGATGTAT
GATCCCAAAATGAATGCTTCTTTTCACTTAAAGTAAAGAGAAAAATTAATCCGGAGTGGTACAAAGGAGAACCAATTTGGGTACAGCTAAGTATCAAGGCCTCAAGTCTGGCACATTTTCTG
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GACCACATTTTACACTTTGATTTTGGAAAGAACCATGATTTCTTCAGGTCTATCATATGACCAGTCAGCAGTGAAGTTCATAAAGCCTTCGAGAGGGTTGATGGTATGGTATGCTGATGGAT
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CCTTCACAAAGAAACCCAGAGATAACCTTGGCTGCTCATGTAAACCCTTCCATTTTGGCGATTGAGGATTTTCAAAACACAGTTCAATCTGACCTGCGCAAGTTCATTAAGCATGAAAACCTT
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AGGTCTCCAAACAAAGCCCTCCAGCCCTCATCGAGAAACCATCTCCAAAGCCAAAGGGCAGCCCGAGAACCAAGGTGTACACCTGCCCCCATCCCCGGGAGGAGATGACCAAGAACCCAGG
TCAGCCTGACCTGCTGCTCAAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCGAGCCGGAGAACAACTACAAGACCAAGCTCCCGTGTGACTCCGACGGCTCCT
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GGGTAATGA (SEQ ID NO: 21)

Fig. 28

MGVLLTQRTLLSLVLALLFPSMASMPSCAKEVKSCKGRCFERTFGNCRCDAAACVELGNCCLDYQETCIEPEHIWTCNKFRCGEKRLTRSLCACSD
CKDKGDDCCINYSVVCQGEKSWVEEPCESINEPQCPAGFETPTLLFSLDGFRAEYLHTWGGLLPVISKLKCGTYTKNMRPVYPTKTFPNHYSIVT
GLYPESHGIIIDNKMYDPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFFWPGSDVEINGIFPDIYKMYNGSVPFEEERILAVLQWLQLPK
DERPHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMMLMDGLKELNLHRCNLILISDHGMEQGSCKKIYILNKYLGDVKNIKVIYGPAAARL
RPSDVDPKYYSFNYESGIARNLSCREPNQHFKPYLKHFLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSEKRYCGSGFHGSDNVFSNMQALFVGyGP
GFKHGIEADTFENIEVYNLMCDLLNLTAPNNGTHGSLNHLKPNVYTPKHPKEVHPLVQCPFTRNPRDNLGCSCNPSILPIEDFQTQFNLTVAEE
KIIKHETLPYGRPRVLQENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTEDFSNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQL
NKNSSGIYSEALLTTNIVPMYQSFQVIWRYFHDITLLRKYAEERNGVNVVSGPVDFDYDGRCDSELENLRQKRRVIRNQEILLPTHFFIVILTSCKDT
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PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
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Fig. 29