Figure 1

DNA sequence of the N-terminal endostatin-albumin fusion open reading frame

ATGAAGTGGGTTTTCATCGTCTCCATTTTGTTCTTGTTCTCCTCTGCTTACTCTA
GATCTTTGGATAAGAGACACAGCCACCGCGACTTCCAGCCGGTGCTCCACCTG
GTTGCGCTCAACAGCCCCCTGTCAGGCGGCATGCGGGGCATCCGCGGGGCCG
ACTTCCAGTGCTTCCAGCAGGCGCGGGCCGTGGGGCTGGCGGGCACCTTCCGC
GCCTTCCTGTCCTCGCGCCTGCAGGACCTGTACAGCATCGTGCGCCGTGCCGA
CCGCGCAGCCGTGCCCATCGTCAACCTCAAGGACGAGCTGCTGTTTCCCAGCT
GGGAGGCTCTGTTCTCAGGCTCTGAGGGTCCGCTGAAGCCCGGGGCACGCATC
TTCTCCTTTGACGGCAAGGACGTCCTGAGGCACCCCACCTGGCCCCAGAAGAG
CGTGTGGCATGGCTCGGACCCCAACGGGCGCAGGCTGACCGAGAGCTACTGT
GAGACGTGGCGGACGGAGGCTCCCTCGGCCACGGGCCAGGCCTCCTCGCTGCT
GGGGGGCAGGCTCCTGGGGCAGAGTGCCGCGAGCTGCCATCACGCCTACATC
GTGCTCTGCATTGAGAACAGCTTCATGACTGCCTCCAAGGACGCTCACAAGTC
CGAAGTCGCTCACCGGTTCAAGGACCTAGGTGAGGAAAACTTCAAGGCTTTGG
TCTTGATCGCTTTCGCTCAATACTTGCAACAATGTCCATTCGAAGATCACGTCA
AGTTGGTCAACGAAGTTACCGAATTCGCTAAGACTTGTGTTGCTGACGAATCT
GCTGAAAACTGTGACAAGTCCTTGCACACCTTGTTCGGTGATAAGTTGTGTAC
TGTTGCTACCTTGAGAGAAACCTACGGTGAAATGGCTGACTGTTGTGCTAAGC
AAGAACCAGAAAGAAACGAATGTTTCTTGCAACACAAGGACGACAACCCAAA
CTTGCCAAGATTGGTTAGACCAGAAGTTGACGTCATGTGTACTGCTTTCCACG
ACAACGAAGAAACCTTCTTGAAGAAGTACTTGTACGAAATTGCTAGAAGACA
CCCATACTTCTACGCTCCAGAATTGTTGTTCTTCGCTAAGAGATACAAGGCTGC
TTTCACCGAATGTTGTCAAGCTGCTGATAAGGCTGCTTGTTTGTTGCCAAAGTT
GGATGAATTGAGAGACGAAGGTAAGGCTTCTTCCGCTAAGCAAAGATTGAAG
TGTGCTTCCTTGCAAAAGTTCGGTGAAAGAGCTTTCAAGGCTTGGGCTGTCGC
TAGATTGTCTCAAAGATTCCCAAAGGCTGAATTCGCTGAAGTTTCTAAGTTGG
TTACTGACTTGACTAAGGTTCACACTGAATGTTGTCACGGTGACTTGTTGGAAT
GTGCTGATGACAGAGCTGACTTGGCTAAGTACATCTGTGAAAACCAAGACTCT
ATCTCTTCCAAGTTGAAGGAATGTTGTGAAAAGCCATTGTTGGAAAAGTCTCA
CTGTATTGCTGAAGTTGAAAACGATGAAATGCCAGCTGACTTGCCATCTTTGG
CTGCTGACTTCGTTGAATCTAAGGACGTTTGTAAGAACTACGCTGAAGCTAAG
GACGTCTTCTTGGGTATGTTCTTGTACGAATACGCTAGAAGACACCCAGACTA
CTCCGTTGTCTTGTTGTTGAGATTGGCTAAGACCTACGAAACTACCTTGGAAA
AGTGTTGTGCTGCTGCTGACCCACACGAATGTTACGCTAAGGTTTTCGATGAA
TTCAAGCCATTGGTCGAAGAACCACAAAACTTGATCAAGCAAAACTGTGAATT
GTTCGAACAATTGGGTGAATACAAGTTCCAAAACGCTTTGTTGGTTAGATACA
CTAAGAAGGTCCCACAAGTCTCCACCCCAACTTTGGTTGAAGTCTCTAGAAAC
TTGGGTAAGGTCGGTTCTAAGTGTTGTAAGCACCCAGAAGCTAAGAGAATGCC
ATGTGCTGAAGATTACTTGTCCGTCGTTTTGAACCAATTGTGTGTTTTGCACGA
AAAGACCCCAGTCTCTGATAGAGTCACCAAGTGTTGTACTGAATCTTTGGTTA
ACAGAAGACCATGTTTCTCTGCTTTGGAAGTCGACGAAACTTACGTTCCAAAG
GAATTCAACGCTGAAACTTTCACCTTCCACGCTGATATCTGTACCTTGTCCGAA
AAGGAAAGACAAATTAAGAAGCAAACTGCTTTGGTTGAATTGGTCAAGCACA
AGCCAAAGGCTACTAAGGAACAATTGAAGGCTGTCATGGATGATTTCGCTGCT

TTCGTTGAAAAGTGTTGTAAGGCTGATGATAAGGAAACTTGTTTCGCTGAAGA
AGGTAAGAAGTTGGTCGCTGCTTCCCAAGCTGCTTTGGGTTTG (SEQ ID NO:30)

Figure 1 con't.

Figure 2

Amino acid sequence of the N-terminal endostatin-albumin fusion protein

MKWVFIVSILFLFSSAYSRSLDKRHSHRDFQPVLHLVALNSPLSGGMRGIRGADFQ
CFQQARAVGLAGTFRAFLSSRLQDLYSIVRRADRAAVPIVNLKDELLFPSWEALFS
GSEGPLKPGARIFSFDGKDVLRHPTWPQKSVWHGSDPNGRRLTESYCETWRTEAP
SATGQASSLLGGRLLGQSAASCHHAYIVLCIENSFMTASKDAHKSEVAHRFKDLG
EENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLF
GDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM
CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACL
LPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVS
KLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKS
HCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDY
SVVLLLRLAKTYETTLEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFE
QLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAE
DYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAE
TFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCK
ADDKETCFAEEGKKLVAASQAALGL (SEQ ID NO:31)

Figure 3

DNA sequence of the C-terminal albumin-endostatin fusion open reading frame

ATGAAGTGGGTAAGCTTTATTTCCCTTCTTTTTCTCTTTAGCTCGGCTTATTCC
AGGAGCTTGGATAAAAGAGATGCACACAAGAGTGAGGTTGCTCATCGGTTT
AAAGATTTGGGAGAAGAAAATTTCAAAGCCTTGGTGTTGATTGCCTTTGCTC
AGTATCTTCAGCAGTGTCCATTTGAAGATCATGTAAAATTAGTGAATGAAGT
AACTGAATTTGCAAAAACATGTGTTGCTGATGAGTCAGCTGAAAATTGTGAC
AAATCACTTCATACCCTTTTTGGAGACAAATTATGCACAGTTGCAACTCTTCG
TGAAACCTATGGTGAAATGGCTGACTGCTGTGCAAAACAAGAACCTGAGAG
AAATGAATGCTTCTTGCAACACAAAGATGACAACCCAAACCTCCCCCGATTG
GTGAGACCAGAGGTTGATGTGATGTGCACTGCTTTTCATGACAATGAAGAGA
CATTTTTGAAAAAATACTTATATGAAATTGCCAGAAGACATCCTTACTTTTAT
GCCCCGGAACTCCTTTTCTTTGCTAAAAGGTATAAAGCTGCTTTTACAGAATG
TTGCCAAGCTGCTGATAAAGCTGCCTGCCTGTTGCCAAAGCTCGATGAACTT
CGGGATGAAGGGAAGGCTTCGTCTGCCAAACAGAGACTCAAGTGTGCCAGT
CTCCAAAAATTTGGAGAAAGAGCTTTCAAAGCATGGGCAGTAGCTCGCCTGA
GCCAGAGATTTCCCAAAGCTGAGTTTGCAGAAGTTTCCAAGTTAGTGACAGA
TCTTACCAAAGTCCACACGGAATGCTGCCATGGAGATCTGCTTGAATGTGCT
GATGACAGGGCGGACCTTGCCAAGTATATCTGTGAAAATCAAGATTCGATCT
CCAGTAAACTGAAGGAATGCTGTGAAAAACCTCTGTTGGAAAAATCCCACTG
CATTGCCGAAGTGGAAAATGATGAGATGCCTGCTGACTTGCCTTCATTAGCT
GCTGATTTTGTTGAAAGTAAGGATGTTTGCAAAAACTATGCTGAGGCAAAGG
ATGTCTTCCTGGGCATGTTTTTGTATGAATATGCAAGAAGGCATCCTGATTAC
TCTGTCGTGCTGCTGCTGAGACTTGCCAAGACATATGAAACCACTCTAGAGA
AGTGCTGTGCCGCTGCAGATCCTCATGAATGCTATGCCAAAGTGTTCGATGA
ATTTAAACCTCTTGTGGAAGAGCCTCAGAATTTAATCAAACAAAATTGTGAG
CTTTTTGAGCAGCTTGGAGAGTACAAATTCCAGAATGCGCTATTAGTTCGTT
ACACCAAGAAAGTACCCCAAGTGTCAACTCCAACTCTTGTAGAGGTCTCAAG
AAACCTAGGAAAAGTGGGCAGCAAATGTTGTAAACATCCTGAAGCAAAAAG
AATGCCCTGTGCAGAAGACTATCTATCCGTGGTCCTGAACCAGTTATGTGTG
TTGCATGAGAAAACGCCAGTAAGTGACAGAGTCACCAAATGCTGCACAGAA
TCCTTGGTGAACAGGCGACCATGCTTTTCAGCTCTGGAAGTCGATGAAACAT
ACGTTCCCAAAGAGTTTAATGCTGAAACATTCACCTTCCATGCAGATATATG
CACACTTTCTGAGAAGGAGAGACAAATCAAGAAACAAACTGCACTTGTTGA
GCTCGTGAAACACAAGCCCAAGGCAACAAAAGAGCAACTGAAAGCTGTTAT
GGATGATTTCGCAGCTTTTGTAGAGAAGTGCTGCAAGGCTGACGATAAGGAG
ACCTGCTTTGCCGAGGAGGGTAAAAAACTTGTTGCTGCAAGTCAAGCTGCCT
TAGGCTTACACAGCCACCGCGACTTCCAGCCGGTGCTCCACCTGGTTGCGCT
CAACAGCCCCCTGTCAGGCGGCATGCGGGGCATCCGCGGGGCCGACTTCCA
GTGCTTCCAGCAGGCGCGGGCCGTGGGGCTGGCGGGCACCTTCCGCGCCTTC
CTGTCCTCGCGCCTGCAGGACCTGTACAGCATCGTGCGCCGTGCCGACCGCG
CAGCCGTGCCCATCGTCAACCTCAAGGACGAGCTGCTGTTTCCCAGCTGGGA
GGCTCTGTTCTCAGGCTCTGAGGGTCCGCTGAAGCCCGGGGCACGCATCTTC
TCCTTTGACGGCAAGGACGTCCTGAGGCACCCCACCTGGCCCCAGAAGAGCG
TGTGGCATGGCTCGGACCCCAACGGGCGCAGGCTGACCGAGAGCTACTGTG

AGACGTGGCGGACGGAGGCTCCCTCGGCCACGGGCCAGGCCTCCTCGCTGCT
GGGGGGCAGGCTCCTGGGGCAGAGTGCCGCGAGCTGCCATCACGCCTACAT
CGTGCTCTGCATTGAGAACAGCTTCATGACTGCCTCCAAG (SEQ ID NO:32)

FIG 3 cont'd.

Figure 4

Amino acid sequence of the C-terminal albumin-endostatin fusion protein

MKWVSFISLLFLFSSAYSRSLDKRDAHKSEVAHRFKDLGEENFKALVLIAFAQYL
QQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYG
EMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYL
YEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSA
KQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG
DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPS
LAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE
KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTK
KVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKT
PVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIK
KQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVA
ASQAALGLHSHRDFQPVLHLVALNSPLSGGMRGIRGADFQCFQQARAVGLAGTF
RAFLSSRLQDLYSIVRRADRAAVPIVNLKDELLFPSWEALFSGSEGPLKPGARIFSF
DGKDVLRHPTWPQKSVWHGSDPNGRRLTESYCETWRTEAPSATGQASSLLGGRL
LGQSAASCHHAYIVLCIENSFMTASK (SEQ ID NO:33)

Figure 5

DNA sequence of the N-terminal angiostatin(non-glycosylated)-albumin fusion open reading frame

ATGAAGTGGGTTTTCATCGTCTCCATTTTGTTCTTGTTCTCCTCTGCTTACTCT
AGATCTTTGGATAAGAGAGTGTATCTCTCAGAGTGCAAGACTGGGAATGGA
AAGAACTACAGAGGGACGATGTCCAAAACAAAAAATGGCATCACCTGTCAA
AAATGGAGTTCCACTTCTCCCCACAGACCTAGATTCTCACCTGCTACACACC
CCTCAGAGGGACTGGAGGAGAACTACTGCAGGAATCCAGACAACGATCCGC
AGGGGCCCTGGTGCTATACTACTGATCCAGAAAAGAGATATGACTACTGCGA
CATTCTTGAGTGTGAAGAGGAATGTATGCATTGCAGTGGAGAAAACTATGAC
GGCAAAATTTCCAAGACCATGTCTGGACTGGAATGCCAGGCCTGGGACTCTC
AGAGCCCACACGCTCATGGATACATTCCTTCCAAATTTCCAAACAAGAACCT
GAAGAAGAATTACTGTCGTAACCCCGATAGGGAGCTGCGGCCTTGGTGTTTC
ACCACCGACCCCAACAAGCGCTGGGAACTTTGTGACATCCCCCGCTGCACAA
CACCTCCACCATCTTCTGGTCCCACCTACCAGTGTCTGAAGGGAACAGGTGA
AAACTATCGCGGGAATGTGGCTGTTACCGTGTCCGGGCACACCTGTCAGCAC
TGGAGTGCACAGACCCCTCACACACATCAAAGGACACCAGAAAACTTCCCCT
GCAAAAATTTGGATGAAAACTACTGCCGCAATCCTGACGGAAAAAGGGCCC
CATGGTGCCATACAACCAACAGCCAAGTGCGGTGGGAGTACTGTAAGATAC
CGTCCTGTGACTCCTCCCCAGTAGACGCTCACAAGTCCGAAGTCGCTCATCG
ATTCAAGGACCTAGGTGAGGAAAACTTCAAGGCTTTGGTCTTGATCGCTTTC
GCTCAATACTTGCAACAATGTCCATTCGAAGATCACGTCAAGTTGGTCAACG
AAGTTACCGAATTCGCTAAGACTTGTGTTGCTGACGAATCTGCTGAAAACTG
TGACAAGTCCTTGCACACCTTGTTCGGTGATAAGTTGTGTACTGTTGCTACCT
TGAGAGAAACCTACGGTGAAATGGCTGACTGTTGTGCTAAGCAAGAACCAG
AAAGAAACGAATGTTTCTTGCAACACAAGGACGACAACCCAAACTTGCCAA
GATTGGTTAGACCAGAAGTTGACGTCATGTGTACTGCTTTCCACGACAACGA
AGAAACCTTCTTGAAGAAGTACTTGTACGAAATTGCTAGAAGACACCCATAC
TTCTACGCTCCAGAATTGTTGTTCTTCGCTAAGAGATACAAGGCTGCTTTCAC
CGAATGTTGTCAAGCTGCTGATAAGGCTGCTTGTTTGTTGCCAAAGTTGGAT
GAATTGAGAGACGAAGGTAAGGCTTCTTCCGCTAAGCAAAGATTGAAGTGT
GCTTCCTTGCAAAAGTTCGGTGAAAGAGCTTTCAAGGCTTGGGCTGTCGCTA
GATTGTCTCAAAGATTCCCAAAGGCTGAATTCGCTGAAGTTTCTAAGTTGGT
TACTGACTTGACTAAGGTTCACACTGAATGTTGTCACGGTGACTTGTTGGAA
TGTGCTGATGACAGAGCTGACTTGGCTAAGTACATCTGTGAAAACCAAGACT
CTATCTCTTCCAAGTTGAAGGAATGTTGTGAAAAGCCATTGTTGGAAAAGTC
TCACTGTATTGCTGAAGTTGAAAACGATGAAATGCCAGCTGACTTGCCATCT
TTGGCTGCTGACTTCGTTGAATCTAAGGACGTTTGTAAGAACTACGCTGAAG
CTAAGGACGTCTTCTTGGGTATGTTCTTGTACGAATACGCTAGAAGACACCC
AGACTACTCCGTTGTCTTGTTGTTGAGATTGGCTAAGACCTACGAAACTACCT
TGGAAAAGTGTTGTGCTGCTGCTGACCCACACGAATGTTACGCTAAGGTTTT
CGATGAATTCAAGCCATTGGTCGAAGAACCACAAAACTTGATCAAGCAAAA
CTGTGAATTGTTCGAACAATTGGGTGAATACAAGTTCCAAAACGCTTTGTTG
GTTAGATACACTAAGAAGGTCCCACAAGTCTCCACCCCAACTTTGGTTGAAG
TCTCTAGAAACTTGGGTAAGGTCGGTTCTAAGTGTTGTAAGCACCCAGAAGC

TAAGAGAATGCCATGTGCTGAAGATTACTTGTCCGTCGTTTTGAACCAATTG
TGTGTTTTGCACGAAAAGACCCCAGTCTCTGATAGAGTCACCAAGTGTTGTA
CTGAATCTTTGGTTAACAGAAGACCATGTTTCTCTGCTTTGGAAGTCGACGA
AACTTACGTTCCAAAGGAATTCAACGCTGAAACTTTCACCTTCCACGCTGAT
ATCTGTACCTTGTCCGAAAAGGAAAGACAAATTAAGAAGCAAACTGCTTTGG
TTGAATTGGTCAAGCACAAGCCAAAGGCTACTAAGGAACAATTGAAGGCTG
TCATGGATGATTTCGCTGCTTTCGTTGAAAAGTGTTGTAAGGCTGATGATAA
GGAAACTTGTTTCGCTGAAGAAGGTAAGAAGTTGGTCGCTGCTTCCCAAGCT
GCTTTGGGTTTG (SEQ ID NO:34)

Figure 5 Cont'd.

Figure 6

Amino acid sequence of the N-terminal angiostatin(non-glycosylated)-albumin fusion protein

MKWVFIVSILFLFSSAYSRSLDKRVYLSECKTGNGKNYRGTMSKTKNGITCQKWS
STSPHRPRFSPATHPSEGLEENYCRNPDNDPQGPWCYTTDPEKRYDYCDILECEEE
CMHCSGENYDGKISKTMSGLECQAWDSQSPHAHGYIPSKFPNKNLKKNYCRNPD
RELRPWCFTTDPNKRWELCDIPRCTTPPPSSGPTYQCLKGTGENYRGNVAVTVSG
HTCQHWSAQTPHTHQRTPENFPCKNLDENYCRNPDGKRAPWCHTTNSQVRWEY
CKIPSCDSSPVDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVN
EVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPER
NECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPE
LLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFG
ERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLA
KYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCK
NYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYA
KVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVS
RNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESL
VNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKP
KATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL (SEQ
ID NO:35)

Figure 7

DNA sequence of the C-terminal albumin-angiostatin(non-glycosylated)-fusion open reading frame

ATGAAGTGGGTAAGCTTTATTTCCCTTCTTTTTCTCTTTAGCTCGGCTTATTCC
AGGAGCTTGGATAAAAGAGATGCACACAAGAGTGAGGTTGCTCATCGGTTT
AAAGATTTGGGAGAAGAAAATTTCAAAGCCTTGGTGTTGATTGCCTTTGCTC
AGTATCTTCAGCAGTGTCCATTTGAAGATCATGTAAAATTAGTGAATGAAGT
AACTGAATTTGCAAAAACATGTGTTGCTGATGAGTCAGCTGAAAATTGTGAC
AAATCACTTCATACCCTTTTTGGAGACAAATTATGCACAGTTGCAACTCTTCG
TGAAACCTATGGTGAAATGGCTGACTGCTGTGCAAAACAAGAACCTGAGAG
AAATGAATGCTTCTTGCAACACAAAGATGACAACCCAAACCTCCCCCGATTG
GTGAGACCAGAGGTTGATGTGATGTGCACTGCTTTTCATGACAATGAAGAGA
CATTTTTGAAAAAATACTTATATGAAATTGCCAGAAGACATCCTTACTTTTAT
GCCCCGGAACTCCTTTTCTTTGCTAAAAGGTATAAAGCTGCTTTTACAGAATG
TTGCCAAGCTGCTGATAAAGCTGCCTGCCTGTTGCCAAAGCTCGATGAACTT
CGGGATGAAGGGAAGGCTTCGTCTGCCAAACAGAGACTCAAGTGTGCCAGT
CTCCAAAAATTTGGAGAAAGAGCTTTCAAAGCATGGGCAGTAGCTCGCCTGA
GCCAGAGATTTCCCAAAGCTGAGTTTGCAGAAGTTTCCAAGTTAGTGACAGA
TCTTACCAAAGTCCACACGGAATGCTGCCATGGAGATCTGCTTGAATGTGCT
GATGACAGGGCGGACCTTGCCAAGTATATCTGTGAAAATCAAGATTCGATCT
CCAGTAAACTGAAGGAATGCTGTGAAAAACCTCTGTTGGAAAAATCCCACTG
CATTGCCGAAGTGGAAAATGATGAGATGCCTGCTGACTTGCCTTCATTAGCT
GCTGATTTTGTTGAAAGTAAGGATGTTTGCAAAAACTATGCTGAGGCAAAGG
ATGTCTTCCTGGGCATGTTTTTGTATGAATATGCAAGAAGGCATCCTGATTAC
TCTGTCGTGCTGCTGCTGAGACTTGCCAAGACATATGAAACCACTCTAGAGA
AGTGCTGTGCCGCTGCAGATCCTCATGAATGCTATGCCAAAGTGTTCGATGA
ATTTAAACCTCTTGTGGAAGAGCCTCAGAATTTAATCAAACAAAATTGTGAG
CTTTTTGAGCAGCTTGGAGAGTACAAATTCCAGAATGCGCTATTAGTTCGTT
ACACCAAGAAAGTACCCCAAGTGTCAACTCCAACTCTTGTAGAGGTCTCAAG
AAACCTAGGAAAAGTGGGCAGCAAATGTTGTAAACATCCTGAAGCAAAAAG
AATGCCCTGTGCAGAAGACTATCTATCCGTGGTCCTGAACCAGTTATGTGTG
TTGCATGAGAAAACGCCAGTAAGTGACAGAGTCACCAAATGCTGCACAGAA
TCCTTGGTGAACAGGCGACCATGCTTTTCAGCTCTGGAAGTCGATGAAACAT
ACGTTCCCAAAGAGTTTAATGCTGAAACATTCACCTTCCATGCAGATATATG
CACACTTTCTGAGAAGGAGAGACAAATCAAGAAACAAACTGCACTTGTTGA
GCTCGTGAAACACAAGCCCAAGGCAACAAAAGAGCAACTGAAAGCTGTTAT
GGATGATTTCGCAGCTTTTGTAGAGAAGTGCTGCAAGGCTGACGATAAGGAG
ACCTGCTTTGCCGAGGAGGGTAAAAAACTTGTTGCTGCAAGTCAAGCTGCCT
TAGGCTTAGTGTATCTCTCAGAGTGCAAGACTGGGAATGGAAAGAACTACA
GAGGGACGATGTCCAAAACAAAAAATGGCATCACCTGTCAAAAATGGAGTT
CCACTTCTCCCCACAGACCTAGATTCTCACCTGCTACACACCCCTCAGAGGG
ACTGGAGGAGAACTACTGCAGGAATCCAGACAACGATCCGCAGGGGCCCTG
GTGCTATACTACTGATCCAGAAAAGAGATATGACTACTGCGACATTCTTGAG
TGTGAAGAGGAATGTATGCATTGCAGTGGAGAAAACTATGACGGCAAAATT
TCCAAGACCATGTCTGGACTGGAATGCCAGGCCTGGGACTCTCAGAGCCCAC

ACGCTCATGGATACATTCCTTCCAAATTTCCAAACAAGAACCTGAAGAAGAA
TTACTGTCGTAACCCCGATAGGGAGCTGCGGCCTTGGTGTTTCACCACCGAC
CCCAACAAGCGCTGGGAACTTTGTGACATCCCCCGCTGCACAACACCTCCAC
CATCTTCTGGTCCCACCTACCAGTGTCTGAAGGGAACAGGTGAAAACTATCG
CGGGAATGTGGCTGTTACCGTGTCCGGGCACACCTGTCAGCACTGGAGTGCA
CAGACCCCTCACACACATCAAAGGACACCAGAAAACTTCCCCTGCAAAAATT
TGGATGAAAACTACTGCCGCAATCCTGACGGAAAAAGGGCCCCATGGTGCC
ATACAACCAACAGCCAAGTGCGGTGGGAGTACTGTAAGATACCGTCCTGTG
ACTCCTCCCCAGTA (SEQ ID NO:36)

Figure 7 Cont'd.

Figure 8

Amino acid sequence of the C-terminal albumin-angiostatin(non-glycosylated)-fusion protein

MKWVSFISLLFLFSSAYSRSLDKRDAHKSEVAHRFKDLGEENFKALVLIAFAQYL
QQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYG
EMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYL
YEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSA
KQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG
DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPS
LAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE
KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTK
KVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKT
PVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIK
KQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVA
ASQAALGLVYLSECKTGNGKNYRGTMSKTKNGITCQKWSSTSPHRPRFSPATHPS
EGLEENYCRNPDNDPQGPWCYTTDPEKRYDYCDILECEEECMHCSGENYDGKIS
KTMSGLECQAWDSQSPHAHGYIPSKFPNKNLKKNYCRNPDRELRPWCFTTDPNK
RWELCDIPRCTTPPPSSGPTYQCLKGTGENYRGNVAVTVSGHTCQHWSAQTPHTH
QRTPENFPCKNLDENYCRNPDGKRAPWCHTTNSQVRWEYCKIPSCDSSPV (SEQ
ID NO:37)

Figure 9

DNA sequence of the N-terminal Kringle5-$(GGS)_4GG$-albumin fusion open reading frame

ATGAAGTGGGTTTTCATCGTCTCCATTTTGTTCTTGTTCTCCTCTGCTTACTCTA
GATCTTTGGATAAGAGATGTATGTTTGGGAATGGGAAAGGATACCGAGGCAA
GAGGGCGACCACTGTTACTGGGACGCCATGCCAGGACTGGGCTGCCCAGGAG
CCCCATAGACACAGCATTTTCACTCCAGAGACAAATCCACGGGCGGGTCTGGA
AAAAAATTACTGCCGTAACCCTGATGGTGATGTAGGTGGTCCCTGGTGCTACA
CGACAAATCCAAGAAAACTTTACGACTACTGTGATGTCCCTCAGTGTGGTGGA
TCCGGTGGTTCCGGTGGTTCTGGTGGTTCCGGTGGTGACGCTCACAAGTCCGA
AGTCGCTCACCGGTTCAAGGACCTAGGTGAGGAAAACTTCAAGGCTTTGGTCT
TGATCGCTTTCGCTCAATACTTGCAACAATGTCCATTCGAAGATCACGTCAAG
TTGGTCAACGAAGTTACCGAATTCGCTAAGACTTGTGTTGCTGACGAATCTGC
TGAAAACTGTGACAAGTCCTTGCACACCTTGTTCGGTGATAAGTTGTGTACTG
TTGCTACCTTGAGAGAAACCTACGGTGAAATGGCTGACTGTTGTGCTAAGCAA
GAACCAGAAAGAAACGAATGTTTCTTGCAACACAAGGACGACAACCCAAACT
TGCCAAGATTGGTTAGACCAGAAGTTGACGTCATGTGTACTGCTTTCCACGAC
AACGAAGAAACCTTCTTGAAGAAGTACTTGTACGAAATTGCTAGAAGACACC
CATACTTCTACGCTCCAGAATTGTTGTTCTTCGCTAAGAGATACAAGGCTGCTT
TCACCGAATGTTGTCAAGCTGCTGATAAGGCTGCTTGTTTGTTGCCAAAGTTG
GATGAATTGAGAGACGAAGGTAAGGCTTCTTCCGCTAAGCAAAGATTGAAGT
GTGCTTCCTTGCAAAAGTTCGGTGAAAGAGCTTTCAAGGCTTGGGCTGTCGCT
AGATTGTCTCAAAGATTCCCAAAGGCTGAATTCGCTGAAGTTTCTAAGTTGGT
TACTGACTTGACTAAGGTTCACACTGAATGTTGTCACGGTGACTTGTTGGAAT
GTGCTGATGACAGAGCTGACTTGGCTAAGTACATCTGTGAAAACCAAGACTCT
ATCTCTTCCAAGTTGAAGGAATGTTGTGAAAAGCCATTGTTGGAAAAGTCTCA
CTGTATTGCTGAAGTTGAAAACGATGAAATGCCAGCTGACTTGCCATCTTTGG
CTGCTGACTTCGTTGAATCTAAGGACGTTTGTAAGAACTACGCTGAAGCTAAG
GACGTCTTCTTGGGTATGTTCTTGTACGAATACGCTAGAAGACACCCAGACTA
CTCCGTTGTCTTGTTGTTGAGATTGGCTAAGACCTACGAAACTACCTTGGAAA
AGTGTTGTGCTGCTGCTGACCCACACGAATGTTACGCTAAGGTTTTCGATGAA
TTCAAGCCATTGGTCGAAGAACCACAAAACTTGATCAAGCAAAACTGTGAATT
GTTCGAACAATTGGGTGAATACAAGTTCCAAAACGCTTTGTTGGTTAGATACA
CTAAGAAGGTCCCACAAGTCTCCACCCCAACTTTGGTTGAAGTCTCTAGAAAC
TTGGGTAAGGTCGGTTCTAAGTGTTGTAAGCACCCAGAAGCTAAGAGAATGCC
ATGTGCTGAAGATTACTTGTCCGTCGTTTTGAACCAATTGTGTGTTTTGCACGA
AAAGACCCCAGTCTCTGATAGAGTCACCAAGTGTTGTACTGAATCTTTGGTTA
ACAGAAGACCATGTTTCTCTGCTTTGGAAGTCGACGAAACTTACGTTCCAAAG
GAATTCAACGCTGAAACTTTCACCTTCCACGCTGATATCTGTACCTTGTCCGAA
AAGGAAAGACAAATTAAGAAGCAAACTGCTTTGGTTGAATTGGTCAAGCACA
AGCCAAAGGCTACTAAGGAACAATTGAAGGCTGTCATGGATGATTTCGCTGCT
TTCGTTGAAAAGTGTTGTAAGGCTGATGATAAGGAAACTTGTTTCGCTGAAGA
AGGTAAGAAGTTGGTCGCTGCTTCCCAAGCTGCTTTGGGTTTG (SEQ ID NO:38)

Figure 10

Amino acid sequence of the N-terminal Kringle5-$(GGS)_4$GG-albumin fusion protein

MKWVFIVSILFLFSSAYSRSLDKRCMFGNGKGYRGKRATTVTGTPCQDWAAQEP
HRHSIFTPETNPRAGLEKNYCRNPDGDVGGPWCYTTNPRKLYDYCDVPQCGGSG
GSGGSGGSGGDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVN
EVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPER
NECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPE
LLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFG
ERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLA
KYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCK
NYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYA
KVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVS
RNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESL
VNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKP
KATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL (SEQ
ID NO:39)

Figure 11

DNA sequence of the C-terminal albumin-$(GGS)_4$GG-Kringle5 fusion open reading frame

ATGAAGTGGGTAAGCTTTATTTCCCTTCTTTTTCTCTTTAGCTCGGCTTATTCCA
GGAGCTTGGATAAAAGAGATGCACACAAGAGTGAGGTTGCTCATCGGTTTAA
AGATTTGGGAGAAGAAAATTTCAAAGCCTTGGTGTTGATTGCCTTTGCTCAGT
ATCTTCAGCAGTGTCCATTTGAAGATCATGTAAAATTAGTGAATGAAGTAACT
GAATTTGCAAAAACATGTGTTGCTGATGAGTCAGCTGAAAATTGTGACAAATC
ACTTCATACCCTTTTTGGAGACAAATTATGCACAGTTGCAACTCTTCGTGAAAC
CTATGGTGAAATGGCTGACTGCTGTGCAAAACAAGAACCTGAGAGAAATGAA
TGCTTCTTGCAACACAAAGATGACAACCCAAACCTCCCCCGATTGGTGAGACC
AGAGGTTGATGTGATGTGCACTGCTTTTCATGACAATGAAGAGACATTTTTGA
AAAAATACTTATATGAAATTGCCAGAAGACATCCTTACTTTTATGCCCCGGAA
CTCCTTTTCTTTGCTAAAAGGTATAAAGCTGCTTTTACAGAATGTTGCCAAGCT
GCTGATAAAGCTGCCTGCCTGTTGCCAAAGCTCGATGAACTTCGGGATGAAGG
GAAGGCTTCGTCTGCCAAACAGAGACTCAAGTGTGCCAGTCTCCAAAAATTTG
GAGAAAGAGCTTTCAAAGCATGGGCAGTAGCTCGCCTGAGCCAGAGATTTCC
CAAAGCTGAGTTTGCAGAAGTTTCCAAGTTAGTGACAGATCTTACCAAAGTCC
ACACGGAATGCTGCCATGGAGATCTGCTTGAATGTGCTGATGACAGGGCGGA
CCTTGCCAAGTATATCTGTGAAAATCAAGATTCGATCTCCAGTAAACTGAAGG
AATGCTGTGAAAAACCTCTGTTGGAAAAATCCCACTGCATTGCCGAAGTGGAA
AATGATGAGATGCCTGCTGACTTGCCTTCATTAGCTGCTGATTTTGTTGAAAGT
AAGGATGTTTGCAAAAACTATGCTGAGGCAAAGGATGTCTTCCTGGGCATGTT
TTTGTATGAATATGCAAGAAGGCATCCTGATTACTCTGTCGTGCTGCTGCTGA
GACTTGCCAAGACATATGAAACCACTCTAGAGAAGTGCTGTGCCGCTGCAGAT
CCTCATGAATGCTATGCCAAAGTGTTCGATGAATTTAAACCTCTTGTGGAAGA
GCCTCAGAATTTAATCAAACAAAATTGTGAGCTTTTTGAGCAGCTTGGAGAGT
ACAAATTCCAGAATGCGCTATTAGTTCGTTACACCAAGAAAGTACCCCAAGTG
TCAACTCCAACTCTTGTAGAGGTCTCAAGAAACCTAGGAAAAGTGGGCAGCA
AATGTTGTAAACATCCTGAAGCAAAAAGAATGCCCTGTGCAGAAGACTATCTA
TCCGTGGTCCTGAACCAGTTATGTGTGTTGCATGAGAAAACGCCAGTAAGTGA
CAGAGTCACCAAATGCTGCACAGAATCCTTGGTGAACAGGCGACCATGCTTTT
CAGCTCTGGAAGTCGATGAAACATACGTTCCCAAAGAGTTTAATGCTGAAACA
TTCACCTTCCATGCAGATATATGCACACTTTCTGAGAAGGAGAGACAAATCAA
GAAACAAACTGCACTTGTTGAGCTCGTGAAACACAAGCCCAAGGCAACAAAA
GAGCAACTGAAAGCTGTTATGGATGATTTCGCAGCTTTTGTAGAGAAGTGCTG
CAAGGCTGACGATAAGGAGACCTGCTTTGCCGAGGAGGGTAAAAAACTTGTT
GCTGCAAGTCAAGCTGCCTTAGGCTTAGGTGGTTCTGGTGGTTCCGGTGGTTCT
GGTGGATCCGGTGGTTGTATGTTTGGGAATGGGAAAGGATACCGAGGCAAGA
GGGCGACCACTGTTACTGGGACGCCATGCCAGGACTGGGCTGCCCAGGAGCC
CCATAGACACAGCATTTTCACTCCAGAGACAAATCCACGGGCGGGTCTGGAA
AAAAATTACTGCCGTAACCCTGATGGTGATGTAGGTGGTCCCTGGTGCTACAC
GACAAATCCAAGAAAACTTTACGACTACTGTGATGTCCCTCAGTGT (SEQ ID NO:40)

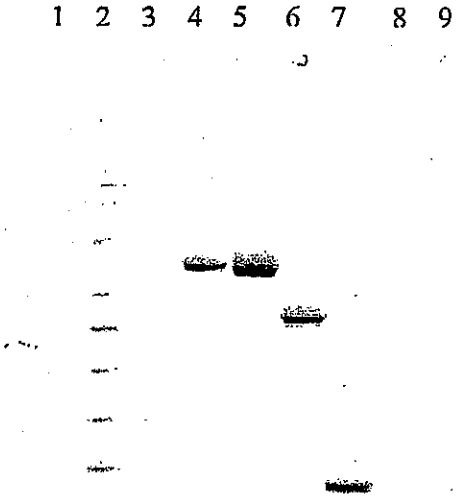
Figure 12

Amino acid sequence of the C-terminal albumin-$(GGS)_4$GG-Kringle5 fusion protein

MKWVSFISLLFLFSSAYSRSLDKRDAHKSEVAHRFKDLGEENFKALVLIAFAQYL
QQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYG
EMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYL
YEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSA
KQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG
DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPS
LAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE
KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTK
KVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKT
PVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIK
KQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVA
ASQAALGLGGSGGSGGSGGSGGCMFGNGKGYRGKRATTVTGTPCQDWAAQEPH
RHSIFTPETNPRAGLEKNYCRNPDGDVGGPWCYTTNPRKLYDYCDVPQC (SEQ
ID NO:41)

Figure 13

A. COLLOIDAL BLUE GEL



Lane	Sample	Load
1.	-	-
2.	Magic Marker	-
3.	-	-
4.	C Terminal Endostatin (1706#45)	1µg
5.	N Terminal Endostatin (1706#49)	1µg
6.	HSA	1µg
7.	Endostatin Standard	1µg
8.	-	-
9.	SPT9901	100ng
10.	-	-

B. ANTI-ENDOSTATIN WESTERN BLOT



C. ANTI-HSA WESTERN BLOT

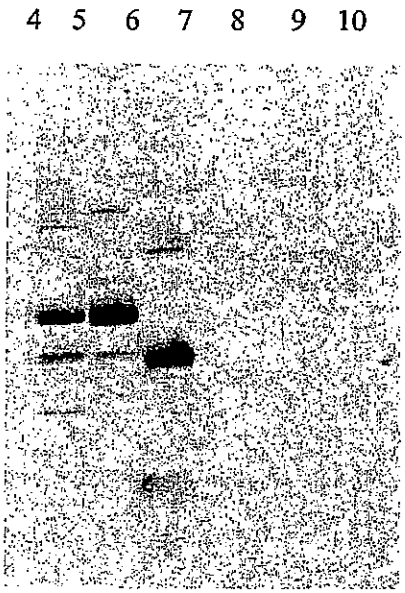


Figure 14

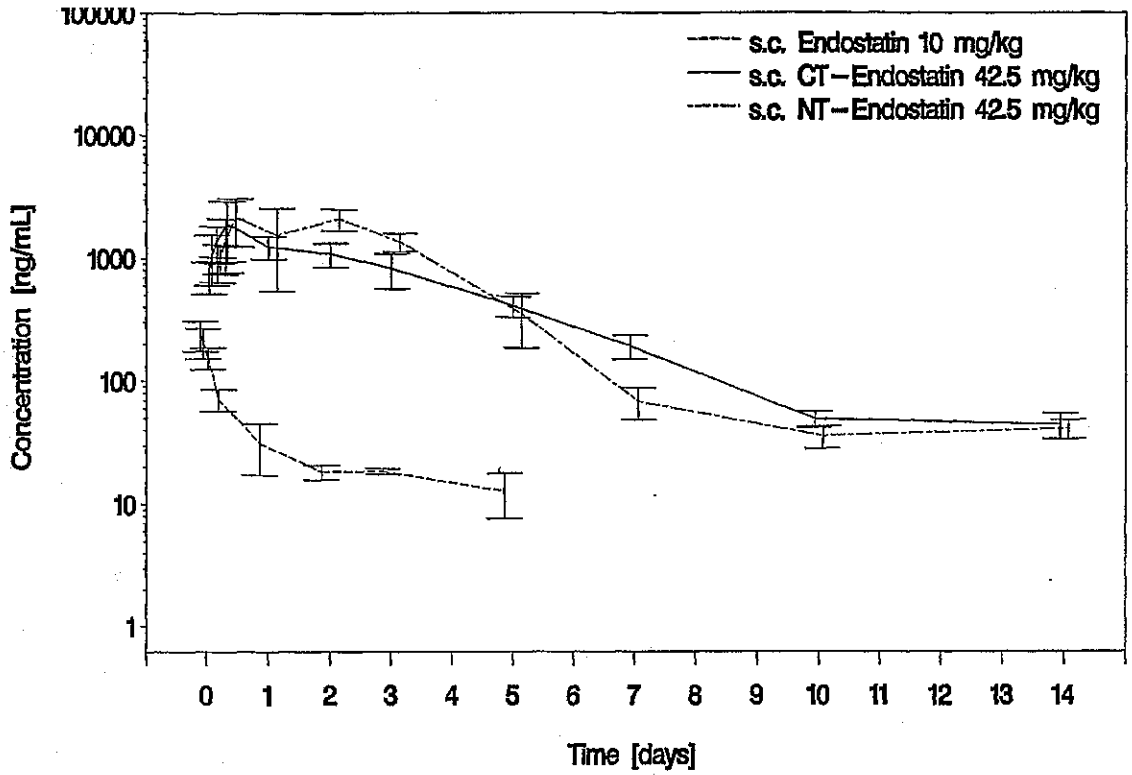

s.c. Endostatin 10 mg/kg
s.c. CT-Endostatin 42.5 mg/kg
s.c. NT-Endostatin 42.5 mg/kg
Concentration [ng/mL]
100000
10000
1000
100
10
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Time [days]

Figure 15

Figure 1: Mean Endostatin concentrations +/− SD, following i.v. application

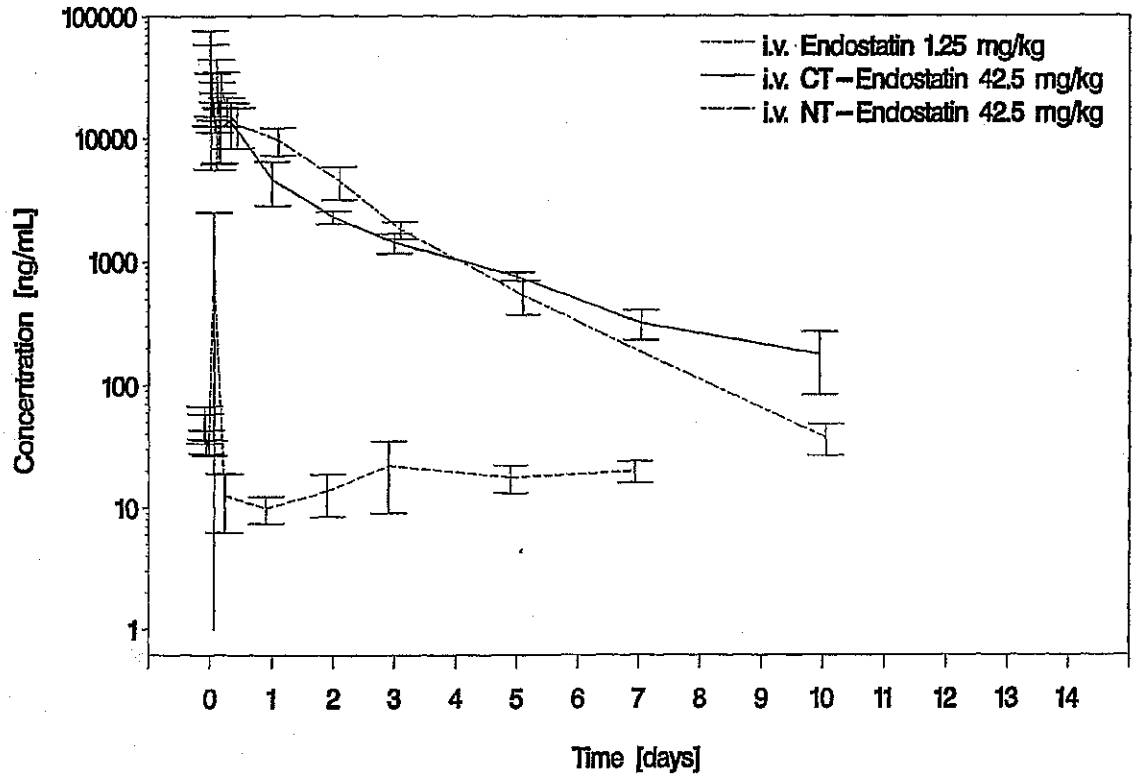


Figure 16

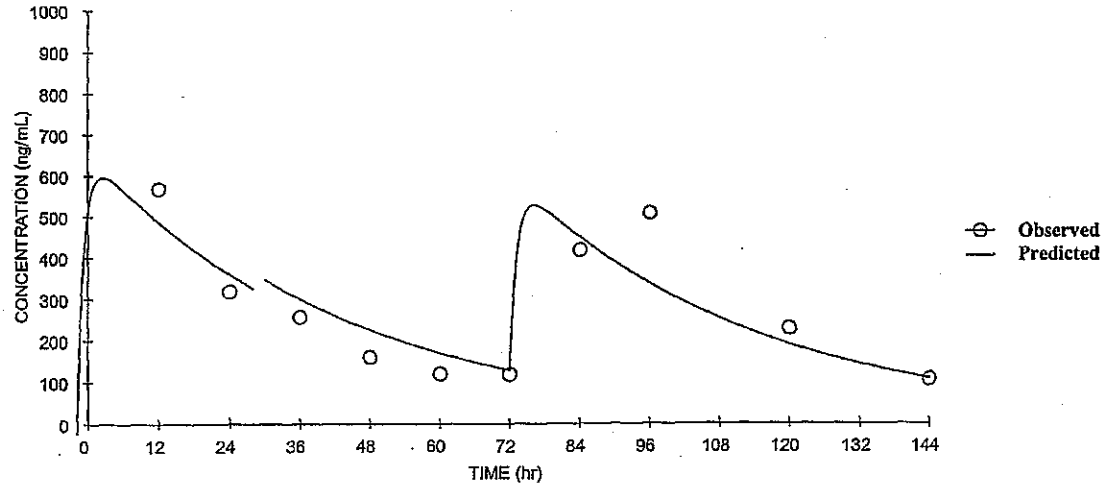

1000
900
800
700
600
500
400
300
200
100
0
CONCENTRATION (ng/mL)
0
12
24
36
48
60
72
84
96
108
120
132
144
TIME (hr)
Observed
Predicted

Figure 17

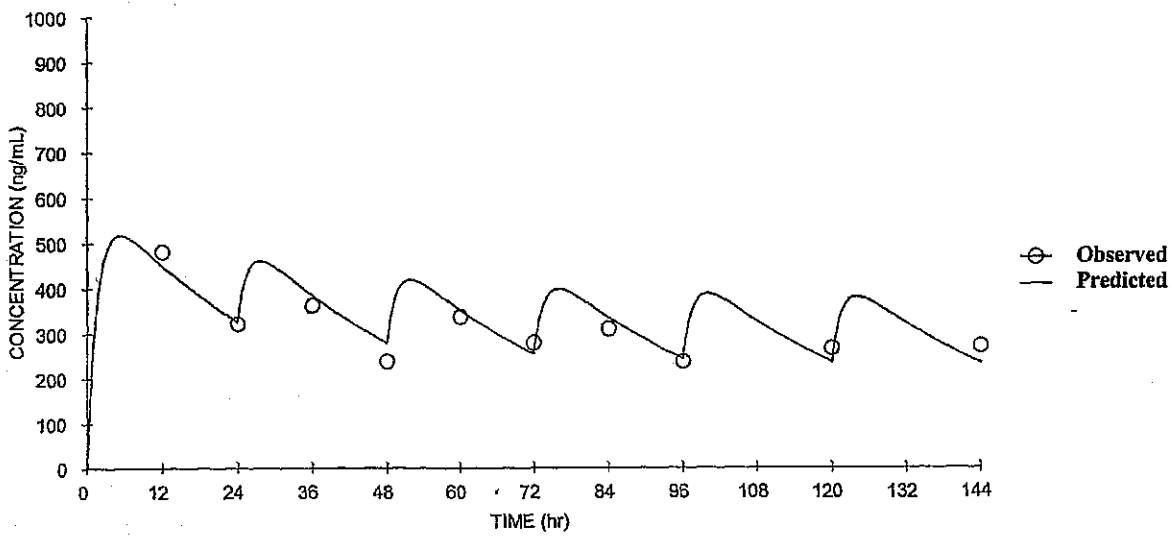

1000
900
800
700
600
500
400
300
200
100
0
CONCENTRATION (ng/mL)
0
12
24
36
48
60
72
84
96
108
120
132
144
TIME (hr)
Observed
Predicted

Figure 18

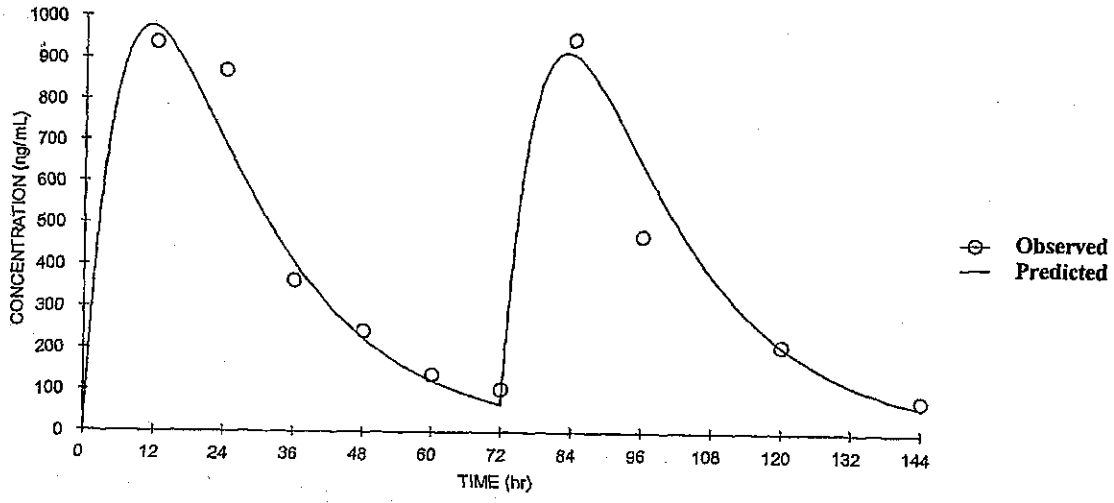

CONCENTRATION (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
12
24
36
48
60
72
84
96
108
120
132
144
TIME (hr)
Observed
Predicted

Figure 19

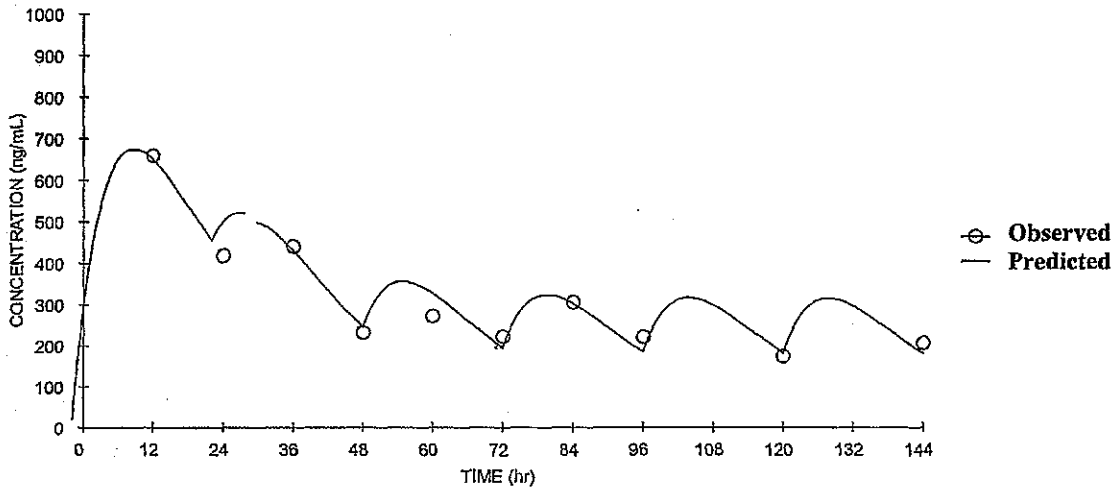

1000
900
800
700
600
500
400
300
200
100
0
CONCENTRATION (ng/mL)
0
12
24
36
48
60
72
84
96
108
120
132
144
TIME (hr)
Observed
Predicted

Figure 20

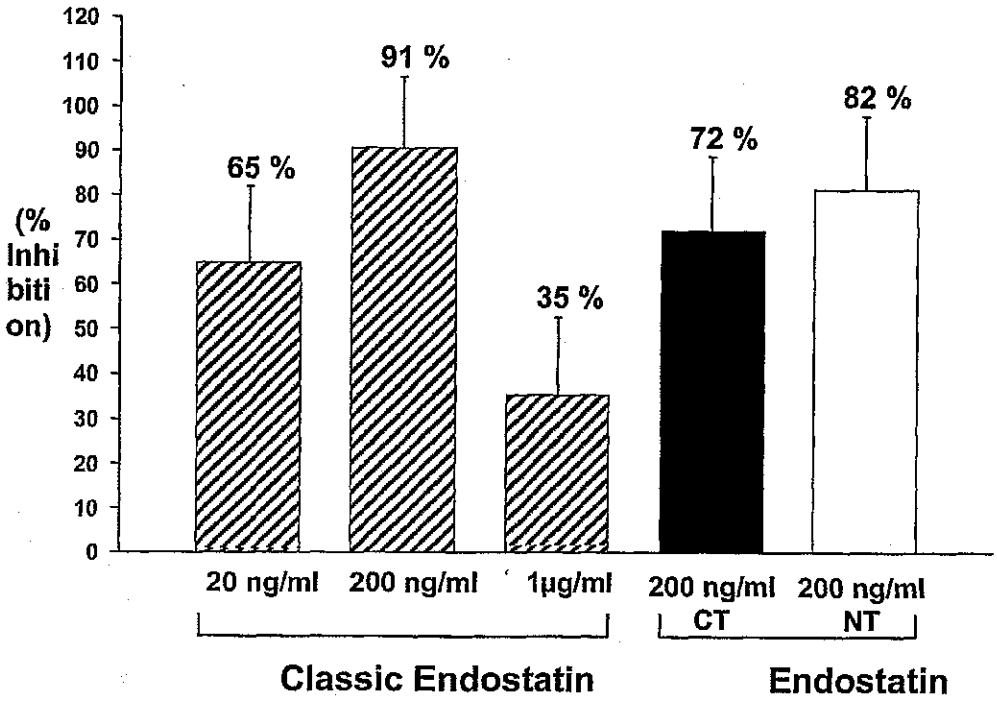

120
110
100
90
80
70
60
50
40
30
20
10
0
(% Inhibition)
65 %
91 %
35 %
72 %
82 %
20 ng/ml
200 ng/ml
1µg/ml
200 ng/ml CT
200 ng/ml NT
Classic Endostatin
Endostatin

Figure 21

Treatment of Bx Pc 3 (Human Pancreatic cancer cell line) with Human AFP-CT- Endostatin s.c.

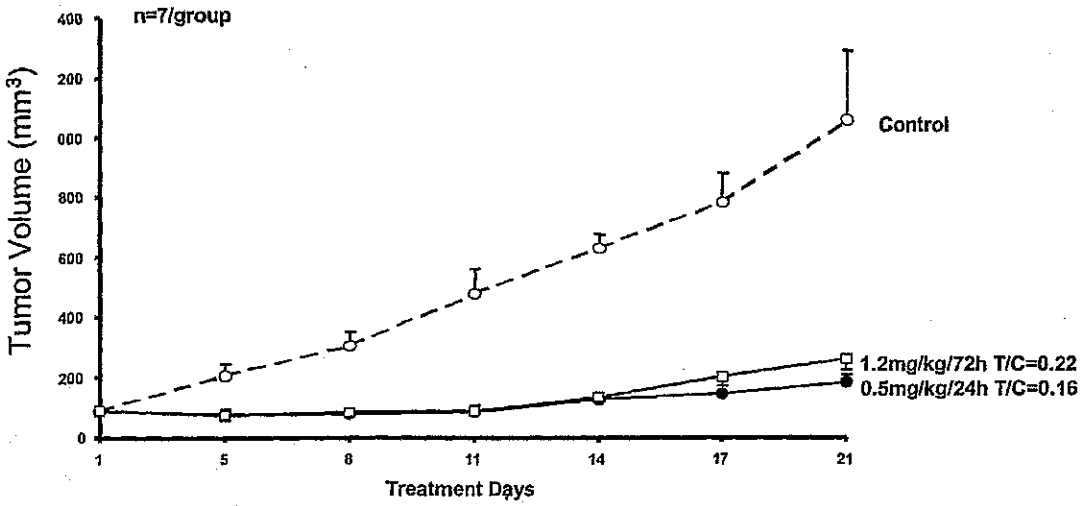


Figure 22

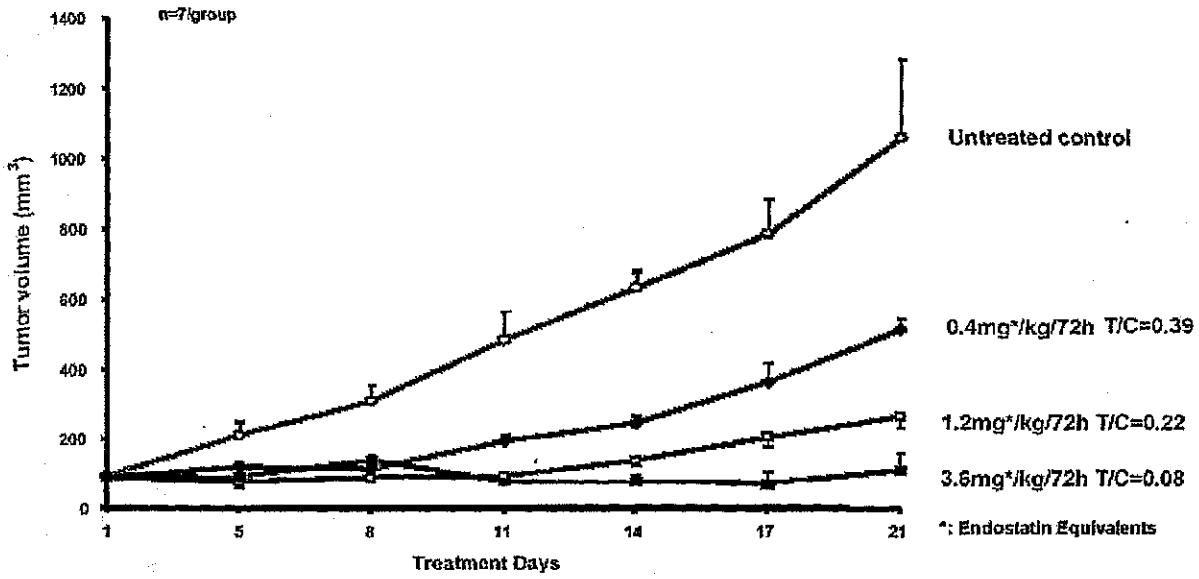

n=7/group
Tumor volume (mm³)
1400
1200
1000
800
600
400
200
0
1
5
8
11
14
17
21
Treatment Days
Untreated control
0.4mg*/kg/72h T/C=0.39
1.2mg*/kg/72h T/C=0.22
3.6mg*/kg/72h T/C=0.08
*: Endostatin Equivalents

Figure 23

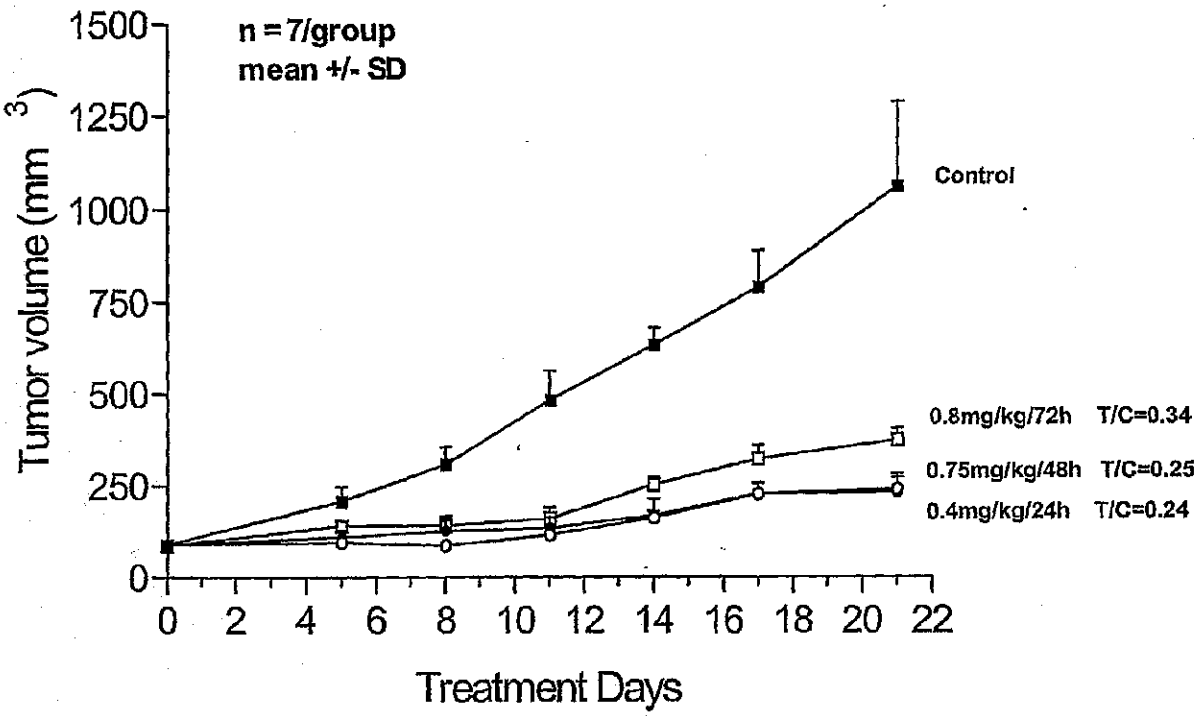

n = 7/group
mean +/- SD
Tumor volume (mm 3)
1500
1250
1000
750
500
250
0
0 2 4 6 8 10 12 14 16 18 20 22
Treatment Days
Control
0.8mg/kg/72h T/C=0.34
0.75mg/kg/48h T/C=0.25
0.4mg/kg/24h T/C=0.24

Figure 24

Treatment of Bx Pc 3 (Human Pancreatic cancer cell line) with Human AFP-NT-Endostatin s.c.

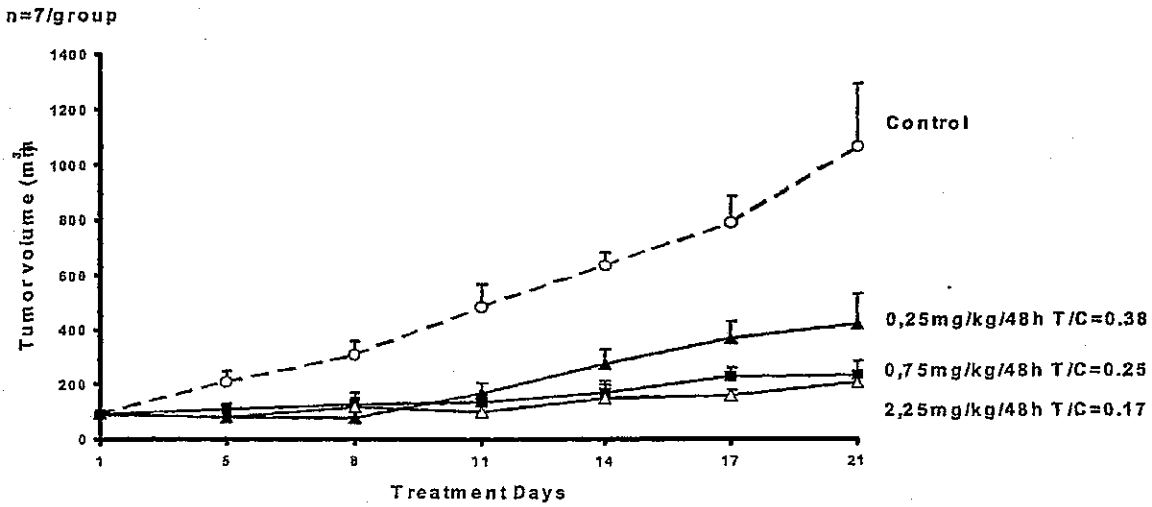
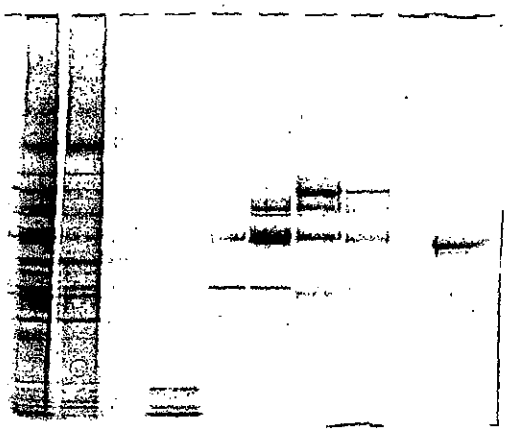


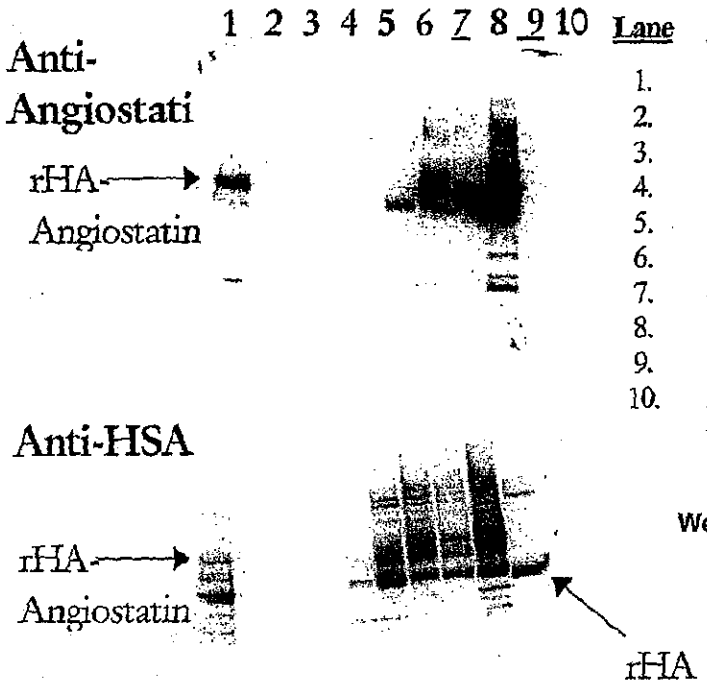
Figure 25



Lane	Sample	Load
1.	C terminal Angiostatin SP-FF Load	nt
2.	Flow Through	nt
3.	Wash 1	nt
4.	Wash 2	nt
5.	Wash 3	nt
6.	Eluate (CS04 + 250mM NaCl)	1µg
7.	Salt Wash	1µg
8.	rHA std (0301_02)	1µg
9.	Eluate (CS04 + 250mM NaCl)	10µg

SDS-PAGE of C-Terminal rHA-Angiostatin on SP-FF

Figure 26

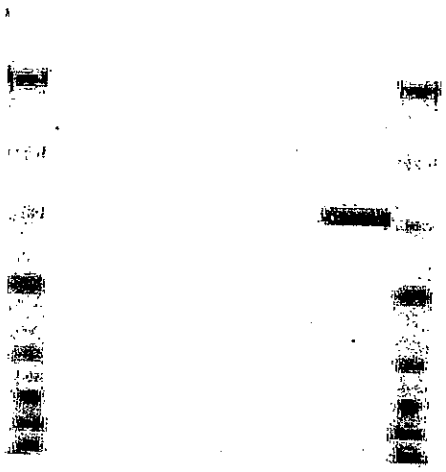


Lane	Sample	Load
1.	C terminal Angiostatin SP-Load	nt
2.	SP-FT	nt
3.	SP-Wash 1	nt
4.	SP-Wash 2	nt
5.	SP-Wash 3	nt
6.	SP-Eluate (CS04)	nt
7.	SP-Eluate (CS04 + 200mM NaCl)	1µg
8.	SP-Salt wash	nt
9.	SP-Eluate (CS04 + 200mM NaCl)	4µg
10.	Angiostatin std	10ng
	rHA std (0301_02)	1µg

Western Blot of C-Terminal rHA-Angiostatin

Figure 27

1 2 3 4 5



```
   1 GAT GCA CAC AAG AGT GAG GTT GCT CAT CGG TTT AAA GAT TTG GGA GAA GAA AAT TTC AAA 60
   1 D   A   H   K   S   E   V   A   H   R   F   K   D   L   G   E   E   N   F   K  20

  61 GCC TTG GTG TTG ATT GCC TTT GCT CAG TAT CTT CAG CAG TGT CCA TTT GAA GAT CAT GTA 120
  21 A   L   V   L   I   A   F   A   Q   Y   L   Q   Q   C   P   F   E   D   H   V  40

 121 AAA TTA GTG AAT GAA GTA ACT GAA TTT GCA AAA ACA TGT GTT GCT GAT GAG TCA GCT GAA 180
  41 K   L   V   N   E   V   T   E   F   A   K   T   C   V   A   D   E   S   A   E  60

 181 AAT TGT GAC AAA TCA CTT CAT ACC CTT TTT GGA GAC AAA TTA TGC ACA GTT GCA ACT CTT 240
  61 N   C   D   K   S   L   H   T   L   F   G   D   K   L   C   T   V   A   T   L  80

 241 CGT GAA ACC TAT GGT GAA ATG GCT GAC TGC TGT GCA AAA CAA GAA CCT GAG AGA AAT GAA 300
  81 R   E   T   Y   G   E   M   A   D   C   C   A   K   Q   E   P   E   R   N   E 100

 301 TGC TTC TTG CAA CAC AAA GAT GAC AAC CCA AAC CTC CCC CGA TTG GTG AGA CCA GAG GTT 360
 101 C   F   L   Q   H   K   D   D   N   P   N   L   P   R   L   V   R   P   E   V 120

 361 GAT GTG ATG TGC ACT GCT TTT CAT GAC AAT GAA GAG ACA TTT TTG AAA AAA TAC TTA TAT 420
 121 D   V   M   C   T   A   F   H   D   N   E   E   T   F   L   K   K   Y   L   Y 140

 421 GAA ATT GCC AGA AGA CAT CCT TAC TTT TAT GCC CCG GAA CTC CTT TTC TTT GCT AAA AGG 480
 141 E   I   A   R   R   H   P   Y   F   Y   A   P   E   L   L   F   F   A   K   R 160
```

Figure 28A

```
481 TAT AAA GCT GCT TTT ACA GAA TGT TGC CAA GCT GCT GAT AAA GCT GCC TGC CTG TTG CCA 540
161 Y   K   A   A   F   T   E   C   C   Q   A   A   D   K   A   A   C   L   L   P 180

541 AAG CTC GAT GAA CTT CGG GAT GAA GGG AAG GCT TCG TCT GCC AAA CAG AGA CTC AAA TGT 600
181 K   L   D   E   L   R   D   E   G   K   A   S   S   A   K   Q   R   L   K   C 200

601 GCC AGT CTC CAA AAA TTT GGA GAA AGA GCT TTC AAA GCA TGG GCA GTG GCT CGC CTG AGC 660
201 A   S   L   Q   K   F   G   E   R   A   F   K   A   W   A   V   A   R   L   S 220

661 CAG AGA TTT CCC AAA GCT GAG TTT GCA GAA GTT TCC AAG TTA GTG ACA GAT CTT ACC AAA 720
221 Q   R   F   P   K   A   E   F   A   E   V   S   K   L   V   T   D   L   T   K 240

721 GTC CAC ACG GAA TGC TGC CAT GGA GAT CTG CTT GAA TGT GCT GAT GAC AGG GCG GAC CTT 780
241 V   H   T   E   C   C   H   G   D   L   L   E   C   A   D   D   R   A   D   L 260

781 GCC AAG TAT ATC TGT GAA AAT CAG GAT TCG ATC TCC AGT AAA CTG AAG GAA TGC TGT GAA 840
261 A   K   Y   I   C   E   N   Q   D   S   I   S   S   K   L   K   E   C   C   E 280

841 AAA CCT CTG TTG GAA AAA TCC CAC TGC ATT GCC GAA GTG GAA AAT GAT GAG ATG CCT GCT 900
281 K   P   L   L   E   K   S   H   C   I   A   E   V   E   N   D   E   M   P   A 300

901 GAC TTG CCT TCA TTA GCT GCT GAT TTT GTT GAA AGT AAG GAT GTT TGC AAA AAC TAT GCT 960
301 D   L   P   S   L   A   A   D   F   V   E   S   K   D   V   C   K   N   Y   A 320
```

Figure 28B

```
 961 GAG GCA AAG GAT GTC TTC CTG GGC ATG TTT TTG TAT GAA TAT GCA AGA AGG CAT CCT GAT 1020
 321 E  A  K  D  V  F  L  G  M  F  L  Y  E  Y  A  R  R  H  P  D  340

1021 TAC TCT GTC GTG CTG CTG AGA CTT GCC AAG ACA TAT GAA ACC ACT CTA GAG AAG TGC 1080
 341 Y  S  V  V  L  L  R  L  A  K  T  Y  E  T  T  L  E  K  C  360

1081 TGT GCC GCT GCA GAT CCT CAT GAA TGC TAT GCC AAA GTG TTC GAT GAA TTT AAA CCT CTT 1140
 361 C  A  A  A  D  P  H  E  C  Y  A  K  V  F  D  E  F  K  P  L  380

1141 GTG GAA GAG CCT CAG AAT TTA ATC AAA CAA AAC TGT GAG CTT TTT GAG CAG CTT GGA GAG 1200
 381 V  E  E  P  Q  N  L  I  K  Q  N  C  E  L  F  E  Q  L  G  E  400

1201 TAC AAA TTC CAG AAT GCG CTA TTA GTT CGT TAC ACC AAG AAA GTA CCC CAA GTG TCA ACT 1260
 401 Y  K  F  Q  N  A  L  L  V  R  Y  T  K  K  V  P  Q  V  S  T  420

1261 CCA ACT CTT GTA GAG GTC TCA AGA AAC CTA GGA AAA GTG GGC AGC AAA TGT TGT AAA CAT 1320
 421 P  T  L  V  E  V  S  R  N  L  G  K  V  G  S  K  C  C  K  H  440

1321 CCT GAA GCA AAA AGA ATG CCC TGT GCA GAA GAC TAT CTA TCC GTG GTC CTG AAC CAG TTA 1380
 441 P  E  A  K  R  M  P  C  A  E  D  Y  L  S  V  V  L  N  Q  L  460

1381 TGT GTG TTG CAT GAG AAA ACG CCA GTA AGT GAC AGA GTC ACA AAA TGC TGC ACA GAG TCC 1440
 461 C  V  L  H  E  K  T  P  V  S  D  R  V  T  K  C  C  T  E  S  480
```

Figure 28C

```
1441 TTG GTG AAC AGG CGA CCA TGC TTT TCA GCT CTG GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500
 481 L   V   N   R   R   P   C   F   S   A   L   E   V   D   E   T   Y   V   P   K   500

1501 GAG TTT AAT GCT GAA ACA TTC ACC TTC CAT GCA GAT ATA TGC ACA CTT TCT GAG AAG GAG 1560
 501 E   F   N   A   E   T   F   T   F   H   A   D   I   C   T   L   S   E   K   E   520

1561 AGA CAA ATC AAG AAA CAA ACT GCA CTT GTT GAG CTT GTG AAA CAC AAG CCC AAG GCA ACA 1620
 521 R   Q   I   K   K   Q   T   A   L   V   E   L   V   K   H   K   P   K   A   T   540

1621 AAA GAG CAA CTG AAA GCT GTT ATG GAT GAT TTC GCA GCT TTT GTA GAG AAG TGC TGC AAG 1680
 541 K   E   Q   L   K   A   V   M   D   D   F   A   A   F   V   E   K   C   C   K   560

1681 GCT GAC GAT AAG GAG ACC TGC TTT GCC GAG GAG GGT AAA AAA CTT GTT GCT GCA AGT CAA 1740
 561 A   D   D   K   E   T   C   F   A   E   E   G   K   K   L   V   A   A   S   Q   580

1741 GCT GCC TTA GGC TTA TAA CAT CTA CAT TTA AAA GCA TCT CAG 1782
 581 A   A   L   G   L   *                                   585
```

Figure 28D