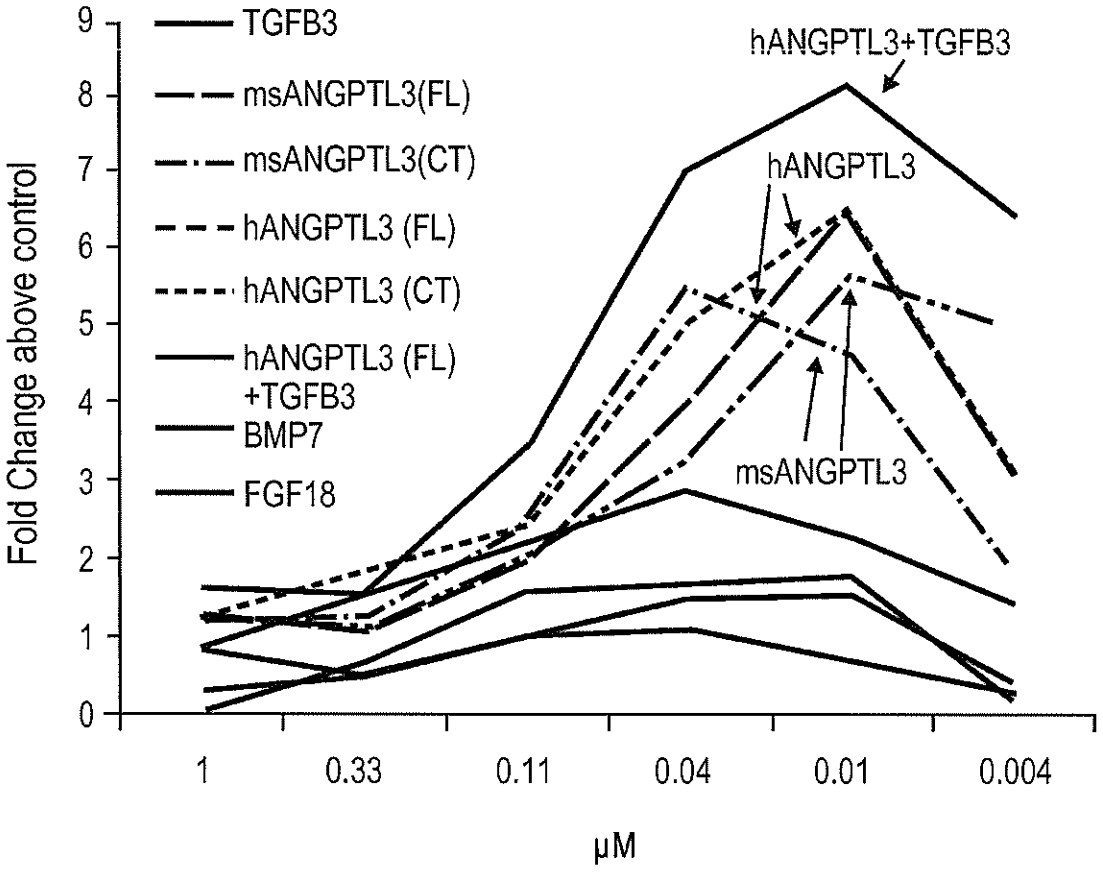

TGFB3
msANGPTL3(FL)
msANGPTL3(CT)
hANGPTL3 (FL)
hANGPTL3 (CT)
hANGPTL3 (FL) +TGFB3
BMP7
FGF18
hANGPTL3+TGFB3
hANGPTL3
msANGPTL3
Fold Change above control
0
1
2
3
4
5
6
7
8
9
1
0.33
0.11
0.04
0.01
0.004
µM

FIG. 1

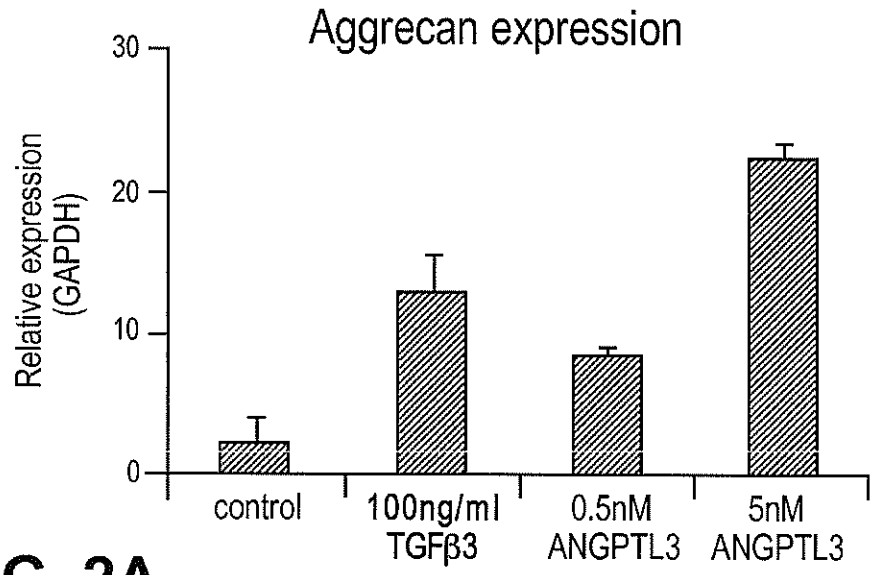


FIG. 2A

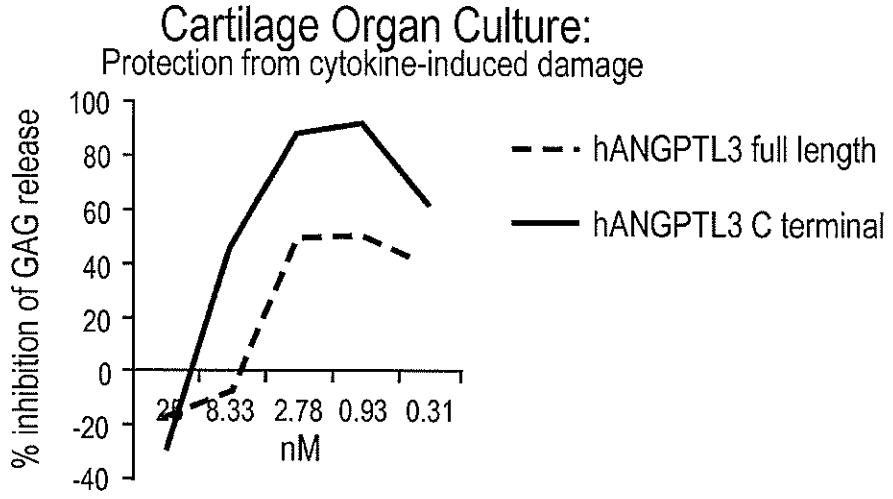


FIG. 2B

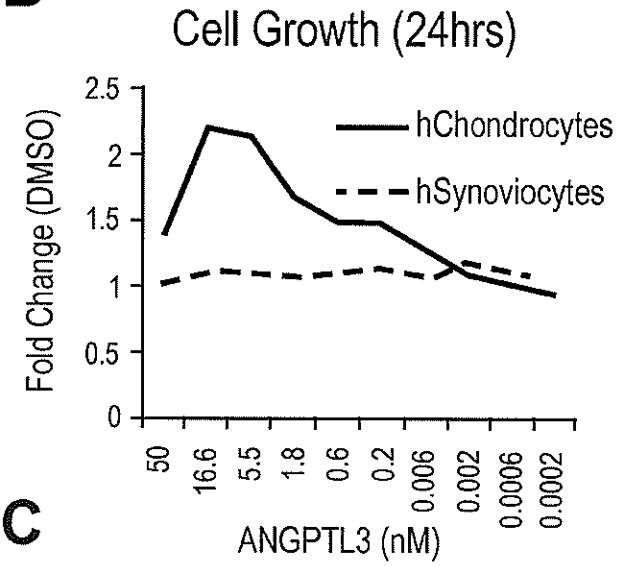


FIG. 2C

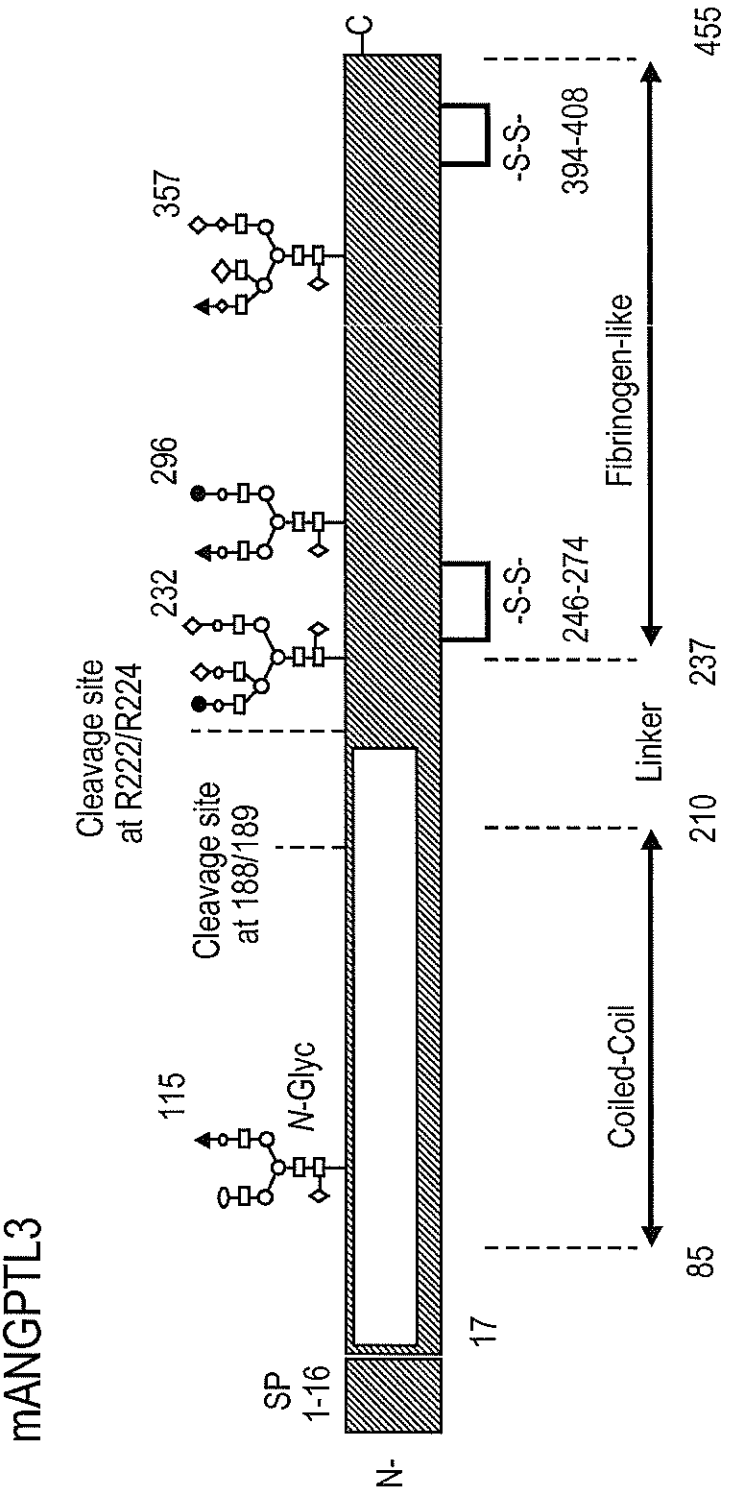

mANGPTL3
SP
1-16
N-
17
C
455
-S-S-
394-408
357
296
232
-S-S-
246-274
Fibrinogen-like
Cleavage site
at R222/R224
Cleavage site
at 188/189
237
Linker
210
115
N-Glyc
Coiled-Coil
85

FIG. 3A

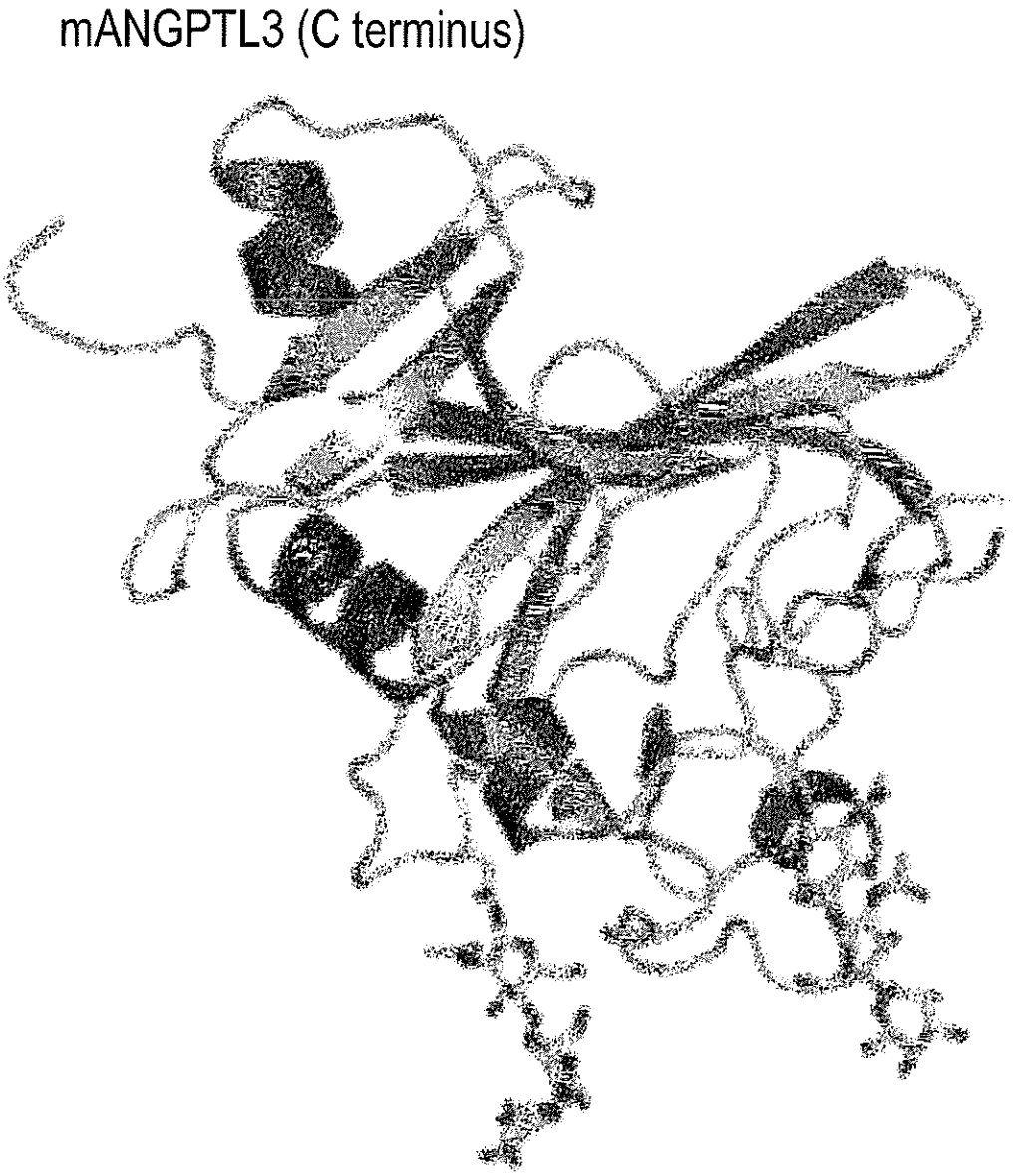


FIG. 3B

```
Bovine      1   MYTIKLFLIIAPLVISSRTDQDYTBLDSTBPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
Canine      1   MYTIKLFLFTIPLVISSKIDRDYSSQYDSVBPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
human       1   MBTIKLLLFTVPLVISSRIDQDNSSFDSLBPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
Mouse       1   MHTIKLFLFVVPLVIASRVDPDLSSFDSAPSEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
consensus       *.*****.*....*****.*..*.*..*.*..**...**********************************************

Bovine     78   FDQSFYDLSLQTNEIKEEEKELRRATSKLQVKNEEVKNMSLELDSKLESLILEEKILLQQKVRYLEDQLTDLIKNQP
Canine     78   FDQSFYDLSLQTNEIKEEEKELRRTTSKLQVKNEEVKNMSLELNSKVESLIEEKILLQQKVRYLEKQLTSLIKNQP
human      78   FDQSFYDLSLQTSEIKEEEKELRRTTYKLQVKNEEVKNMSLELNSKLESLIEEKILLQQKVKBLEEQLTNLIQNQP
Mouse      78   FDQSFYDLSLRTNEIKEEEKELRRTTSTLQVKNEEVKNMSVBLNSKLESLIEEKTALQHKVRALEEQLTNLILSPA
consensus       **********.*.**********.*..*************.**.**.*******..**.*.**..**.***.**....

Bovine    154   QIQEYLEVTSLKTLVEQQDNSIKDLLQIVEEQVRDLNQQQSQIKEIENQLRRTGTKESTEISLSSKPRAPRTTPSF
Canine    154   EIQEHPEVTSLKTFVEQQDNSIKDLLQTVEEQMRDLNQQHSQIKEIENQLR-NVIQESTENSLSSKPRAPRTTPFL
human     154   ETPEHPEVTSLKTTVEKQDNSIKDLLQTVEDVKDLNQQHSQIKEIENQLRRTSIQEPTEISLSSKPRAPRTTPFL
Mouse     154   GAQEHPEVTSLKSFVEQQDNSIREELLQSVEEQMKDLSQQHMQIKEIEKQLRKTGIQEHSENSLSSKSRAPRTTPPL
consensus       ...*..******..**.*****..***.**.**.**.**..*******.***....*.*..* ***** ********..

Bovine    230   HSNETKNVEHDDIPADCTIIYNQGKHTSGIYSIRPSNSQVFNVYCDVKSGSSWTLIQHRIDGSQNFNETWEN
Canine    229   HLNETKNVEHNDIPANCTTIYNRGEHTSGIYSIRPSNSQVFNVYCDVKSGSSWTLIQHRIDGSQNFNETWEN
human     230   QLNEIRNVKHDGIPAETTTIYNRGEHTSGMVAIRPSNSQVFHVYCDVISGSPWTLIQHRIDGSQNFNETWEN
Mouse     230   QLNETENTEQDDLPADQSAVYNRGEHTSQVHTIKPRNSQGFNVYCDTQSGSPWTLIQHRKDGSQDFNETWEN
consensus       .**..*.....**.*...**.*.*****.*.*.*.***.*.****..*** *******.****.*******
```

FIG. 4A

```
Bovine    302 YKYGFGRLDGEFWLGLEKIYSIVQSNYILRIELEDWKD-KYYTEYSFHLGDHETNYTLHLAEISGNGPKAFPEHK
Canine    301 YRYGFGRLDGEFWLGLEKIYSIVKQSNYILRIELEDWNDNKHYIEYTFHLGNHETNYTLHLVEITGNILNALPEHK
human     302 YKYGFGRLDGEFWLGLEKIYSIVKQSNYMLRIELEDWKDNKHYIEYSFYLGNHETNYTLHLVAITGNMPNALPENK
Mouse     302 YEKGFGRLDGEFWLGLEKIYAIVQQSNYILRLELQDWKDSKHYMEYSFHLGSHETNYTLHLAEIAGNIPGALPEHT
consensus     *.*********************.**.****.**.**.*.*.*.*.**.*.**.********  .*.**...*.**..

Bovine    377 DLMFSTWDHKAKGHFNCPESNSGGWWYHDVCGENNLNGKYNKPKAKPERKEGICWKSQDGRLYSIKATKMLIHP
Canine    377 DLVFSTWDHKAKGHVNCPESYSGGWWWHNVCGENNLNGKYNKQRAKTKPERRRQLYWKSQNGRLYSIKSTKMLIHP
human     378 DLVFSTWDHKAKGHFNCPEGYSGGWWWHDECGENNLNGKYNKPRAKSKPERRRQLSWKSQNGRLYSIKSTKMLIHP
Mouse     378 DLMFSTWNHRAKGQLYCPESYSGGWWWNDICGENNLNGKYNKPRTKSRPERRRQLYWEPQSRKLYAIKSSKMLQP
consensus     **.*****.*.***...***..*****.....**************....*..***..*...*....**.**...*

Bovine    453 SDSENSE 459
Canine    453 IDSESSE 459
human     454 TDSESFE 460
Mouse     454 TT----- 455
consensus     ..**..*
```

FIG. 4A (cont.)

```
bovine      1 MYTIKLFLIIAPLVISSRTDQDYTSLDSTSPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
equine      1 MYTIKLFLVIAPLVISSRIDQDYSSLDSIPPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
canine      1 MYTIKLFLFIIPLVISSKIDRDYSSKVDSVSPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
human       1 MFTIKLLLFTVPLVISSRIDQDNSSFDSLSPEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
mouse       1 MHTIKLFLFVVPLVIASRVDPDLSSFDSAPSEPKSRFAMLDDVKILANGLLQLGHGLKDFVHKTKGQINDIFQKLNI
consensus   1 *.*****.*....*****.*..*.*..*.**...**********************************************

bovine     78 FDQSFYDLSLQTNEIKEEEKELRRATSKLQVKNEEVKNMSLELDSKLESLLEEKILLQQKVRYLEDQLTDLIKNQP
equine     78 FDQSFYALSLQTNEIKEEEKELRRTTSKLQVKNEEVKNMSLELNSKLESLLEEKSLLQQKVKYLEEQLTKLIKNQP
canine     78 FDQSFYDLSLQTNEIKEEEKELRRTTSKLQVKNEEVKNMSLELNSKVESLLEEKILLQQKVRYLEKQLTSLIKNQP
human      78 FDQSFYDLSLQTSEIKEEEKELRRTTYKLQVKNEEVKNMSLELNSKLESLLEEKTLLQQKVKYLEEQLTNLIQNQP
mouse      78 FDQSFYDLSLRTNEIKEEEKELRRTTSTLQVKNEEVKNMSVELNSKLESLLEEKTALQHKVRALEEQLTNLILSPA
consensus  81 ******.***.*.**************.*..**************.**.**.*******..**.**..**.*** **.....

bovine    154 QIQEYLEVTSLKTLVEQQDNSIKDLLQIVEEQYRQLNQQQSQIKEIENQLRRTGIKESTEISLSSKPRAPRTTPSF
equine    154 EIQEHPEVTSLKTFVEQQDNSIKDLLQTMEEQYRQLNQQHSQIKEIENQLRRTGIQESTENSLSSKPRAPRTTPSF
canine    154 EIQEHPEVTSLKTFVEQQDNSIKDLLQTVEEQYRQLNQQHSQIKEIENQLR-NVIQESTENSLSSKPRAPRTTPFL
human     154 ETPEHPEVTSLKTFVEKQDNSIKDLLQTVEDQYKQLNQQHSQIKEIENQLRRTSIQEPTEISLSSKPRAPRTTPFL
mouse     154 GAQEHPEVTSLKSFVEQQDNSIREFLLQSVEEQYKQLSQQHMQIKEIEKQLRKTGIQEPSENSLSSKSRAPRTTPPL
consensus 161  ...*..*******..**.******..***.*.**.**.**.*******.***...*.*..*.*.*****.********  .

bovine    230 HSNETKNVEHDDIPADCTIIYNQGKHTSGIYSIRPSNSQVFNVYCDVKSGSSWTLIQHRIDGSQNFNETWEN
equine    230 HLNETKDVEHDDFPADCTTIYNRGEHTSGIYSIKPSNSQVFNVYCDVISGSSWILIQRRIDGSQNFNETWQN
canine    229 HLNETKNVEHNDIPANCTTIYNRGEHTSGIYSIRPSNSQVFNVYCDVKSGSSWTLIQHRIDGSQNFNETWEN
human     230 QLNEIRNVKHDGIPAECTTIYNRGEHTSGMYAIRPSNSQVFHVYCDVISGSPWTLIQHRIDGSQNFNETWEN
mouse     230 QLNETENTEQDDLPADCSAVYNRGEHTSGVMTIKPRNSQGFNVYCDTQSGSPWTLIQHRKDGSQDFNETWEN
consensus 241  ..**.........**.*...**.*.*.*****.*.*.*.***.*.*****. ***.*.***.*.****.*****.*
```

FIG. 4B

```
bovine      302 YKYGFGRLDGEFWLGLEKIYSIVMQSNYILRIELEDWKD-KYYTEYSFHLGDHETNYTLHLAETSGNGPKAFPEHK
equine      302 YKYGFGRLDFEFWLGLEKIYSIVKRSNYIIRIELEDWKDNKHTIEYSFHLGNHETNYTLHLVEITGNVPNALPEHK
canine      301 YRYGFGRLDGEFWLGLEKIYSIVKQSNYILRIELEDWNDNKHYIEYFFHLGNHETNYTLHLVEITGNLLNALPEHK
human       302 YKYGFGRLDGEFWLGLEKIYSIVKQSNYVLRIELEDWKDNKHYIEYSFYLGNHETNYTLHLVAITGNVPNALPENK
mouse       302 YEKGFGRLDGEFWLGLEKIYAIVQQSNYILRLELQDWKDSKHYVEYSFHLGSHETNYTLHVAEIAGNLPGALPEHT
consensus   321 *..*******.**********.**..***.**.**.**.*.*...**.*.**.*********....*.**....*.**..

bovine      377 DIMFSTWDHKAKGHFNCPESNSGGWWYHDVCGENNLNGKYNKPKKAKAKPERKEGICWKSQDGRLYSIKATKMLIHP
equine      378 DLVFSTWDHKAKGQLNCLESYSGGWWWHDVCGGDNPNGKYNKPRSKTKPERRGICWKSQNGRLYTIKSTKMLIHP
canine      377 DLVFSTWDHKAKGHVNCPESYSGGWWWHNVCGENNLNGKYNKQRAKTKPERRGLYWKSQNGRLYSIKSTKMLIHP
human       378 DLVFSTWDHKAKGHFNCPEGYSGGWWWHDECGENNLNGKYNKPRAKSKPERRGLSWKSQNGRLYSIKSTKMLIHP
mouse       378 DIMFSTWNHRAKGQLICPESYSGGWWWNDICGENNLNGKYNKPRTKSRPERRGIYWRPQSRKLYAIKSSKMLQP
consensus   401 **.*****.*.***....*.*..*****.....**..*.*******....*..***..*. *..*....**.**....*

bovine      453 SDSENSE---------- 459
equine      454 IDSESFELRQIKKPMN 469
canine      453 IDSESSE---------- 459
human       454 TDSESFE---------- 460
mouse       454 IT------------- 455
consensus   481 ..**. *
```

FIG. 4B (cont.)

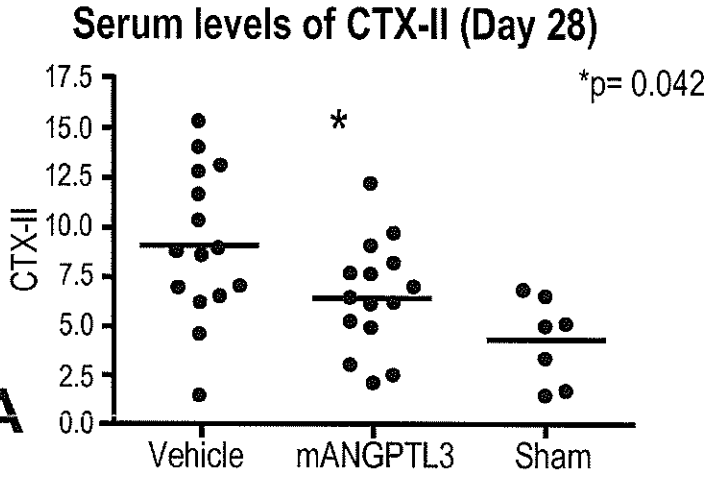


FIG. 5A

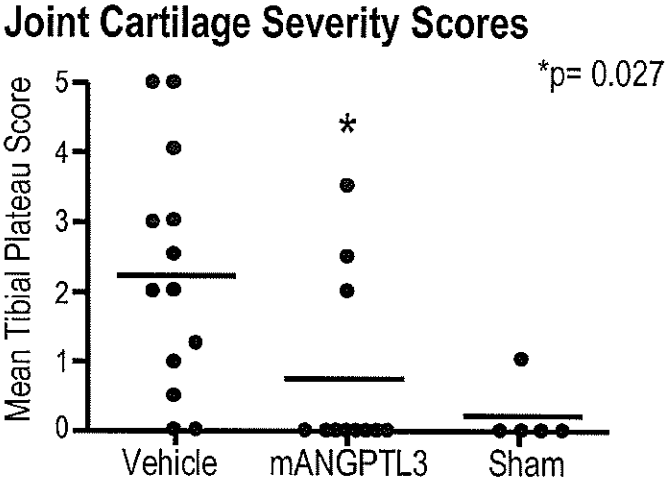


FIG. 5B

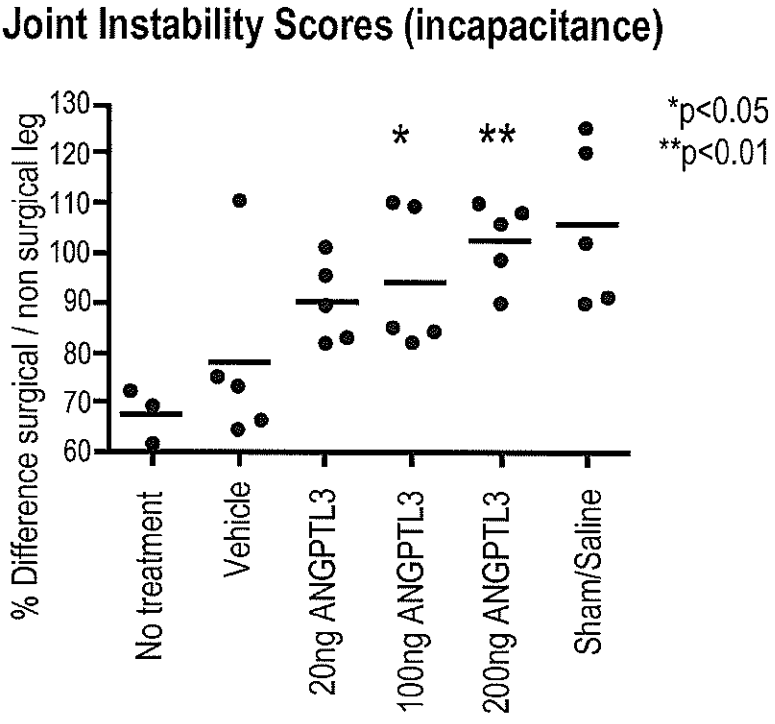


FIG. 5C