

FIGURE 1

α OPGL-1 Heavy Chain cDNA

DNA sequence of heavy chain expression plasmid beginning at HindIII site, through Sall site. Start codon begins at nt 14, stop codon begins at nt 1415.

```
1  AAGCTTGACC ACCATGGAGT TTGGGCTGAG CTGGCTTTTT CTTGTGGCTA TTTTAAAAGG
61  TGTCCAGTGT GAGGTGCAGC TGTTGGAGTC TGGGGGAGGC TTGGTACAGC CTGGGGGGTC
121 CCTGAGACTC TCCTGTGCAG CCTCTGGATT CACCTTTAGC AGCTATGCCA TGAGCTGGGT
181 CCGCCAGGCT CCAGGGAAGG GGCTGGAGTG GGTCTCAGGT ATTACTGGGA GTGGTGGTAG
241 TACATACTAC GCAGACTCCG TGAAGGGCCG GTTCACCATC TCCAGAGACA ATTCCAAGAA
301 CACGCTGTAT CTGCAAATGA ACAGCCTGAG AGCCGAGGAC ACGGCCGTAT ATTACTGTGC
361 GAAAGATCCA GGGACTACGG TGATTATGAG TTGGTTTCGAC CCCTGGGGCC AGGGAACCCCT
421 GGTCACCGTC TCCTCAGCCT CCACCAAGGG CCCATCGGTC TTCCCCCTGG CGCCCTGCTC
481 CAGGAGCACC TCCGAGAGCA CAGCGGCCCT GGGCTGCCTG GTCAAGGACT ACTTCCCCGA
541 ACCGGTGACG GTGTCGTGGA ACTCAGGCGC TCTGACCAGC GGCCTGCACA CCTTCCAGC
601 TGTCCTACAG TCCTCAGGAC TCTACTCCCT CAGCAGCGTG GTGACCGTGC CCTCCAGCAA
661 CTTCGGCACC CAGACCTACA CCTGCAACGT AGATCACAAG CCCAGCAACA CCAAGGTGGA
721 CAAGACAGTT GAGCGCAAAT GTTGTGTCGA GTGCCACCG TGCCCAGCAC CACCTGTGGC
781 AGGACCGTCA GTCTTCCTCT TCCCCCAAAC ACCCAAGGAC ACCCTCATGA TCTCCCGGAC
841 CCCTGAGGTC ACGTGCGTGG TGGTGGACGT GAGCCACGAA GACCCCGAGG TCCAGTTCAA
901 CTGGTACGTG GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCACGGG AGGAGCAGTT
961 CAACAGCACG TTCCGTGTGG TCAGCGTCCT CACCGTTGTG CACCAGGACT GGCTGAACGG
1021 CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGGCCTCCCA GCCCCCATCG AGAAAACCAT
1081 CTCCAAAACC AAAGGGCAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC CATCCCGGGA
1141 GGAGATGACC AAGAACCAGG TCAGCCTGAC CTGCCTGGTC AAAGGCTTCT ACCCCAGCGA
1201 CATCGCCGTG GAGTGGGAGA GCAATGGGCA GCCGGAGAAC AACTACAAGA CCACACCTCC
1261 CATGCTGGAC TCCGACGGCT CTTTCTTCT CTACAGCAAG CTCACCGTGG ACAAGAGCAG
1321 GTGGCAGCAG GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC ACAACCACTA
1381 CACGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATGATAA GTCGAC (SEQ ID NO: 1)
```

FIGURE 2

α OPGL-1 Heavy Chain Amino Acid Sequence

The IgG2 signal peptide is underlined, the variable region is in capital letters and is not underlined, and the constant region is in lower case.

```
1 MEFGLSWLFL VAILKGVOCE VQLLESGGGL VQPGGSLRLS CAASGFTFSS YAMSWVRQAP
61 GKGLEWVSGI TGSGGSTYYA DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKDPG
121 TTVIMSWFDP WGQGTLVTVS Sastkgpsvf plapcsrsts estaaIgclv kdyfpepvtv
181 swnsgaltsg vhtfpavlqs sglyslssvv tvpssnfgtq tytcnvdhkp sntkvdkteve
241 rkccvecppc pappvagpsv flfppkpkdt lmisrtpevt cvvvdvshed pevqfnwyvd
301 gvevhnaktk preeqfnstf rvvsvltvvh qdwlngkeyk ckvsnkglpa piektisktk
361 gqprepvyt lppsreemtk nqvsItclvk gfypsdiave wesngqpenn ykttppmlds
421 dgsfflyskl tvdksrwqqg nvfscsvmhe alhnhytqks lsIspgk (SEQ ID NO: 2)
```

FIGURE 3

α OPGL-1 kappa Light Chain cDNA

DNA sequence of kappa chain expression plasmid sequence from XbaI site through SalI site. Start codon begins at nt 12; stop codon begins at nt 717

```
1 TCTAGACCAC CATGGAAACC CCAGCGCAGC TTCTCTTCCT CCTGCTACTC TGGCTCCCAG
61 ATACCACCGG AGAAATTGTG TTGACGCAGT CTCCAGGCAC CCTGTCTTTG TCTCCAGGGG
121 AAAGAGCCAC CCTCTCCTGT AGGGCCAGTC AGAGTGTTCT CGGCAGGTAC TTAGCCTGGT
181 ACCAGCAGAA ACCTGGCCAG GCTCCCAGGC TCCTCATCTA TGGTGCATCC AGCAGGGCCA
241 CTGGCATCCC AGACAGGTTT AGTGGCAGTG GGTCTGGGAC AGACTTCACT CTCACCATCA
301 GCAGACTGGA GCCTGAAGAT TTTGCAGTGT TTTACTGTCA GCAGTATGGT AGTTCACCTC
361 GGACGTTTCGG CCAAGGGACC AAGGTGGAAA TCAAACGAAC TGTGGCTGCA CCATCTGTCT
421 TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCCTCTGTT GTGTGCCTGC
481 TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT
541 CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC TACAGCCTCA
601 GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC GCCTGCGAAG
661 TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTGAT
721 AAGTCGAC (SEQ ID NO: 3)
```

FIGURE 4

α OPGL-1 kappa Light Chain Amino Acid Sequence

The kappa signal peptide is underlined, the variable region is in capital letters and not underlined, and the constant region is in lower case.

```
1 METPAQLLFL LLLWLPDTTG EIVLTQSPGT LSLSPGERAT LSCRASQSVR
51 GRYLAWYQKK PGQAPRLLIY GASSRATGIP DRFSGSGSGT DFTLTISRLE
101 PEDFAVFYQC QYGSSPRTFG QGTKVEIKrt vaapsvfifp psdeqlksgt
151 asvvcllnnf ypreakvqwk vdnalqsgns qesvteqdsd dstyslsstl
201 tlskadyekh kvyacevthq glsspvtksf nrged (SEQ ID NO: 4)
```

FIGURE 5

Circular Plasmid Map of α OPGL-1-kappa/pDSRa19

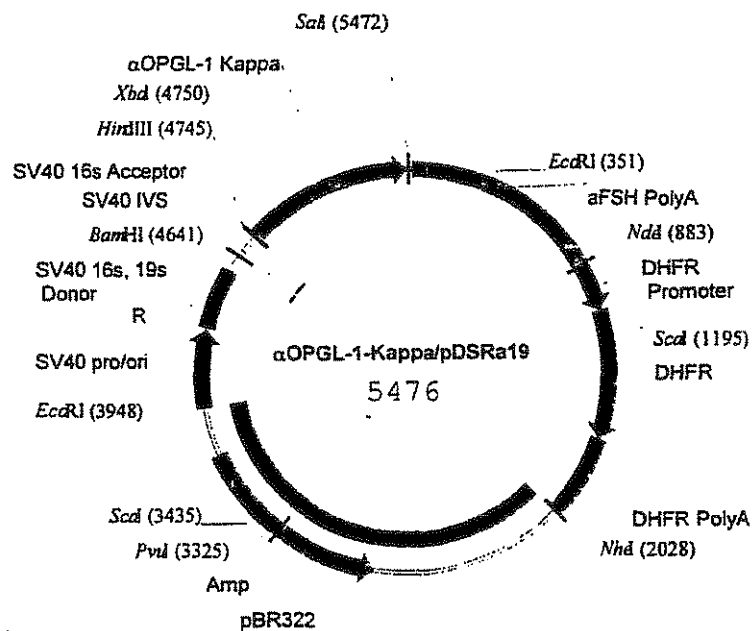


FIGURE 6

Circular Plasmid Map of α OPGL-1-IgG2/pDSR α 19

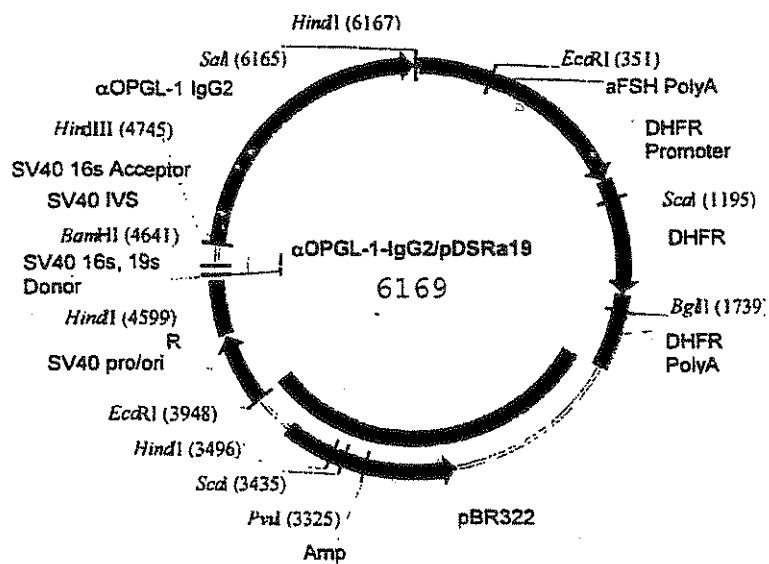
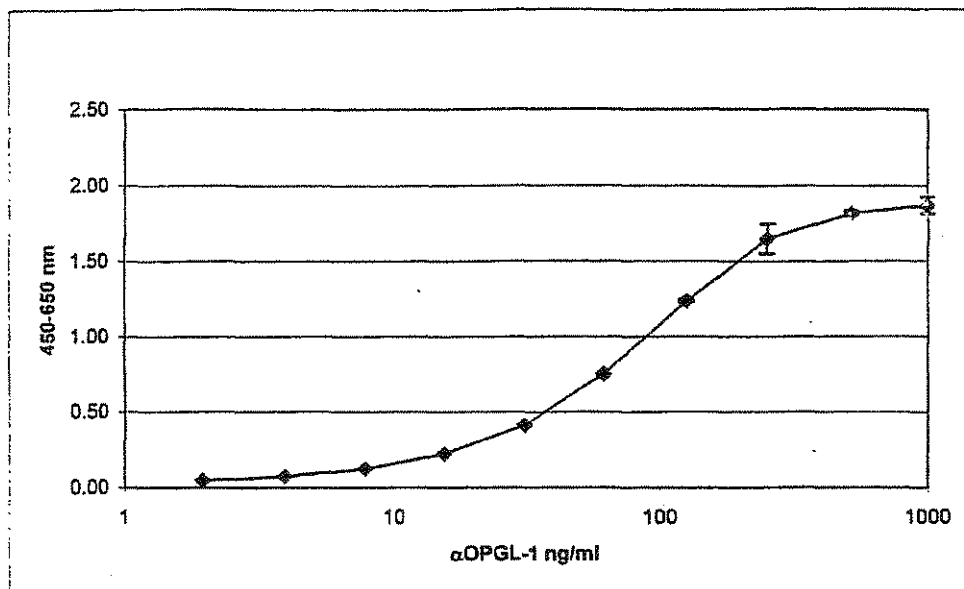


FIGURE 7

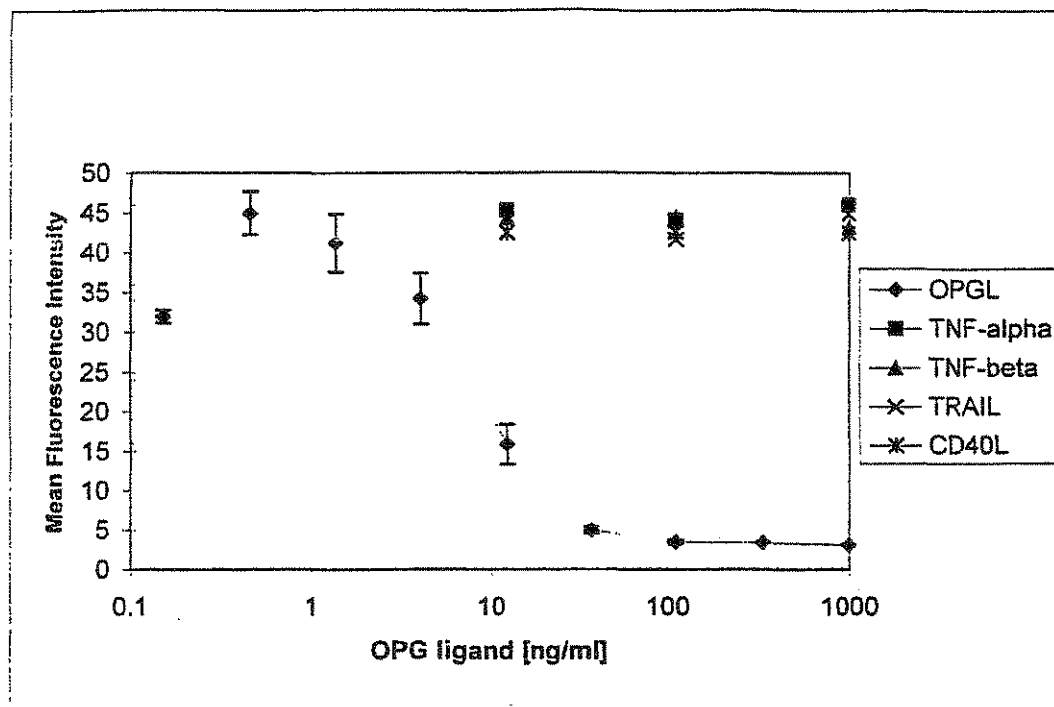
α OPGL-1 Binds to Soluble OPG Ligand Coated on the EIA Plate in a Dose-dependent Manner



96-well EIA plates are coated with recombinant soluble OPG. Varying concentrations of α OPGL-1 are added to the wells and incubated for about 2hrs at room temperature. Bound antibody is detected with goat anti-Human IgG (Fab')-Horse Radish Peroxidase. The absorbance is read at 450 nm and 650 nm.

FIGURE 8

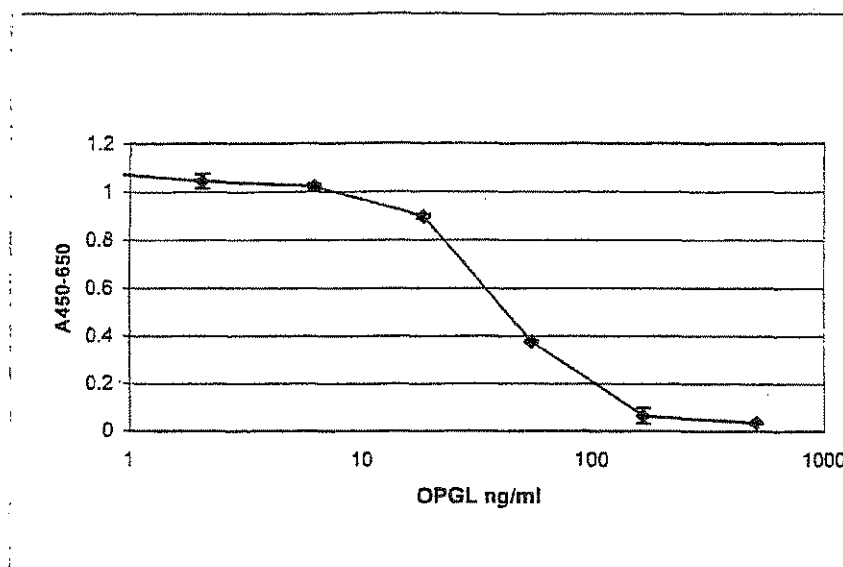
α OPGL-1 Binds Specifically to Membrane-bound OPGL



α OPGL-1 binds to OPGL expressed on a cell surface of transfected CHO REN 218-9 cells in a dose-dependent manner. This binding is competed by exogenously added human OPGL but not by TNF- α , TNF- β , TRAIL or CD40 ligand. α OPGL-1 (100 ng/ml) is pre-incubated with varying concentrations of soluble OPGL or other ligands and is then incubated with CHO REN 218-9 cells expressing OPGL on the surface. Cells are then incubated for 30 minutes at 2-8°C with FITC-labeled F(ab')₂ Goat anti-Human IgG, Fc γ Fragment Specific. After centrifugation and washing cell surface fluorescence is measured using flow cytometry.

FIGURE 9

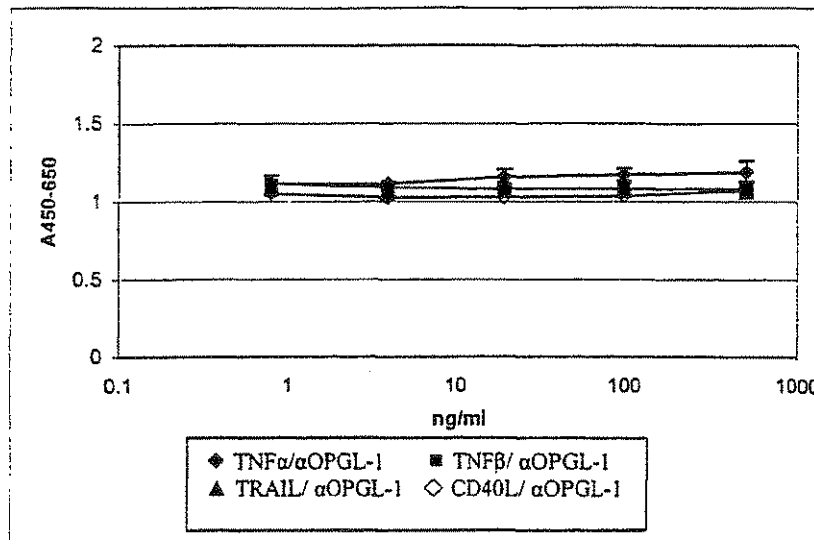
α OPGL-1 Binds to Soluble OPGL



α OPGL-1 binding to OPGL on an EIA plate is reduced competitively by exogenously added soluble OPGL.

Figure 10

α OPGL-1 does not bind to TNF family members TNF α , TNF β , TRAIL, or CD40 ligand



α OPGL-1 binding to OPGL on an EIA plate is not reduced by exogenously added TNF- α , TNF- β , TRAIL or CD40 Ligand.

FIGURE 11

Dose-dependent Inhibition by α OPGL-1 of OPG Ligand-induced TRAP Activity in RAW 264.7 Cells

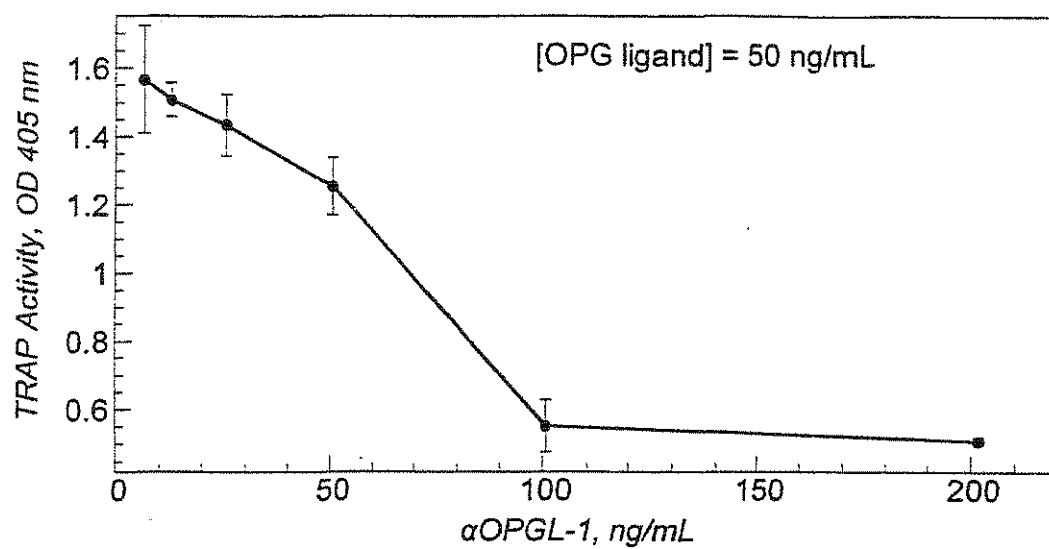


FIGURE 12

Dose-dependent Inhibition by α OPGL-1 of Europium-labeled OPG Ligand Binding to ODAR-FLAG/anti-FLAG-APC

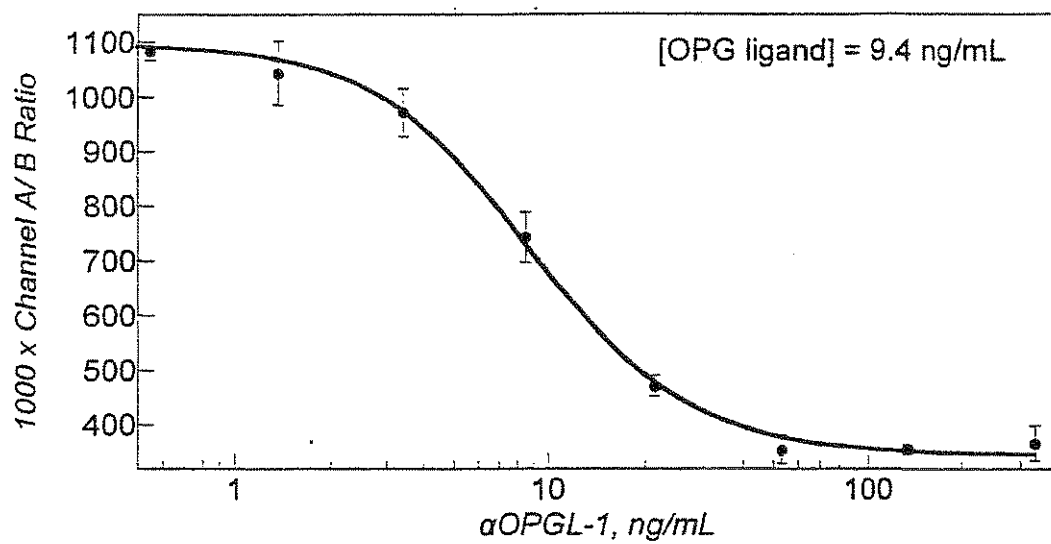


FIGURE 13

Mean ($\pm$ SD) Serum-Concentration Time Profiles Following Single Dose Administration of α OPGL-1 to Cynomolgus Monkeys at Doses of 0.1, 1 and 10.0 mg/kg IV (n=2/dose) and 1.0 mg/kg SC (n=6/dose)

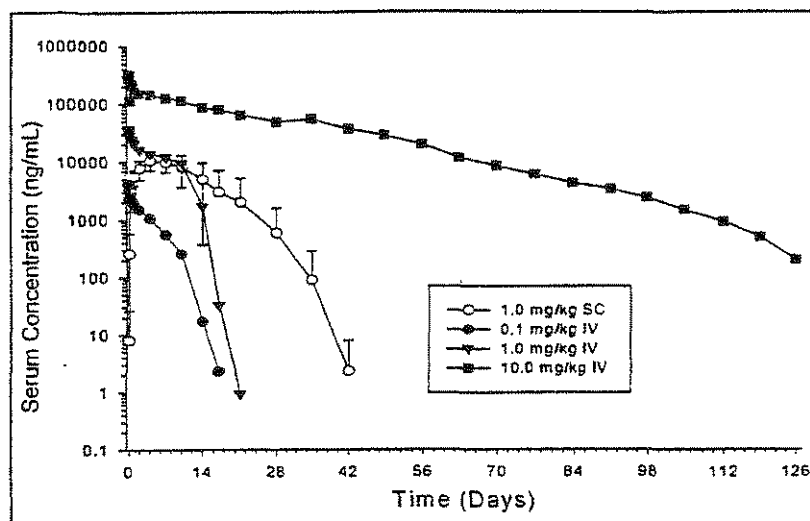


FIGURE 14

Mean ($\pm$ SD) Percent Change in Serum N-Tx Concentration After Administering a Single Dose of α OPGL-1 IV (n=2/dose) or SC (n=6) to Cynomolgus Monkeys at Doses of 0.1, 1 and 10.0 mg/kg.

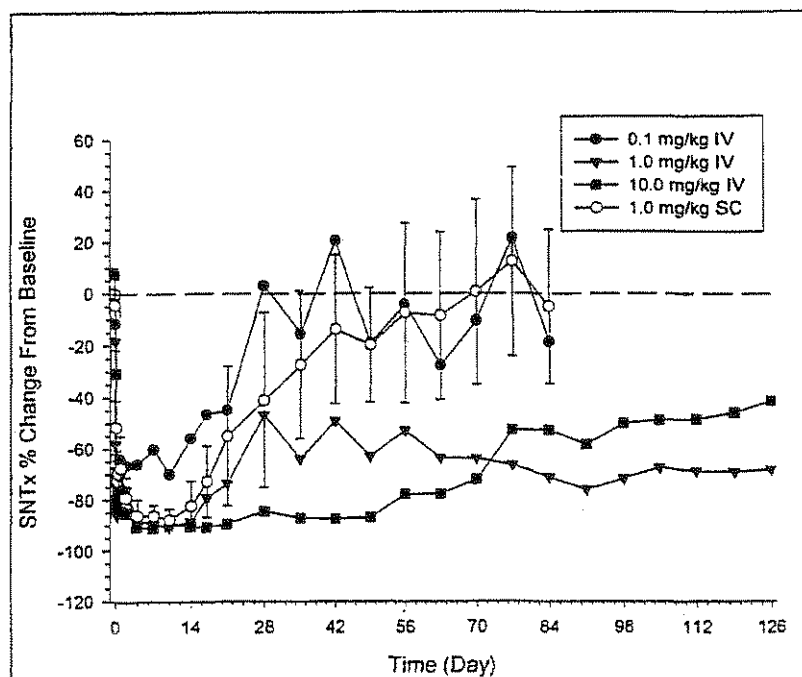


FIGURE 15

Mean ($\pm$ SD) Percent Change in Urine N-Tx Concentration Following Single Dose IV (n=2/dose) or SC (n=6) Administration of α OPGL-1 to Cynomolgus Monkeys at Doses of 0.1, 1 and 10.0 mg/kg

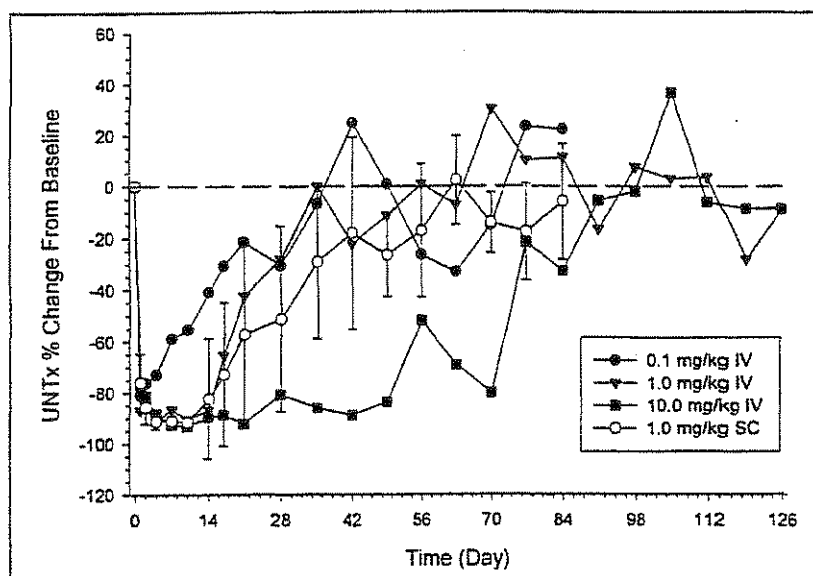


FIGURE 16

**Antibody Positive (open black symbols) and Negative (closed red symbols)
Animal Serum-Concentration Time Profiles After Administering a Single Dose of
 α OPGL-1 IV to Cynomolgus Monkeys at a Dose of 0.1 mg/kg**

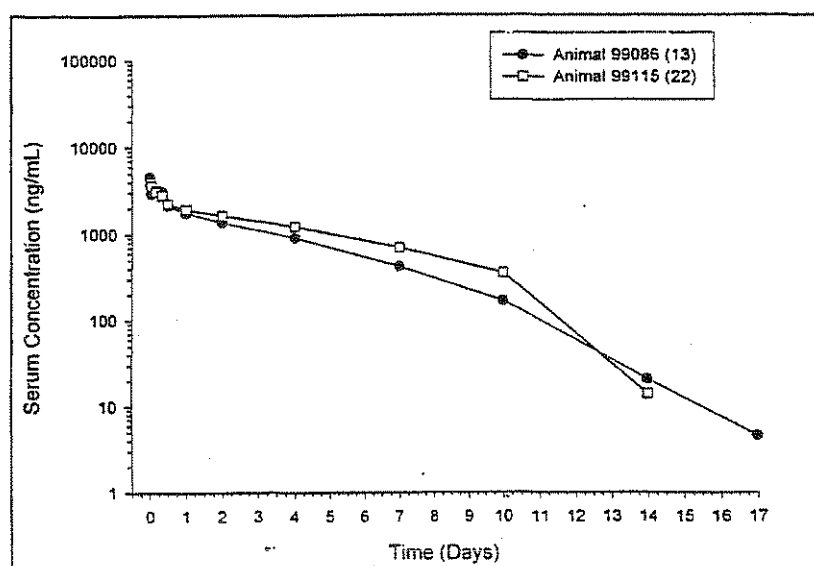


FIGURE 17

α OPGL-1 Heavy Chain Variable Region Amino Acid Sequence

1 EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA
41 PGKGLEWVSG ITGSGGSTYY ADSVKGRFTI SRDNSKNTLY
81 LQMNSLRAED TAVYYCAKDP GTTVIMSWFD PWGQGTLVTV
121 SS (SEQ ID NO: 13)

FIGURE 18

α OPGL-1 Light Chain Variable Region Amino Acid Sequence

1 EIVLTQSPGT LSLSPGERAT LSCRASQSVR GRYLAWYQQK
41 PGQAPRLLIY GASSRATGIP DRFSGSGSGT DFTLTISRLE
81 PEDFAVFYCQ QYGSSPRTEG QGTKVEIK (SEQ ID NO: 14)

FIGURE 19

Cell Culture Process Flow Chart

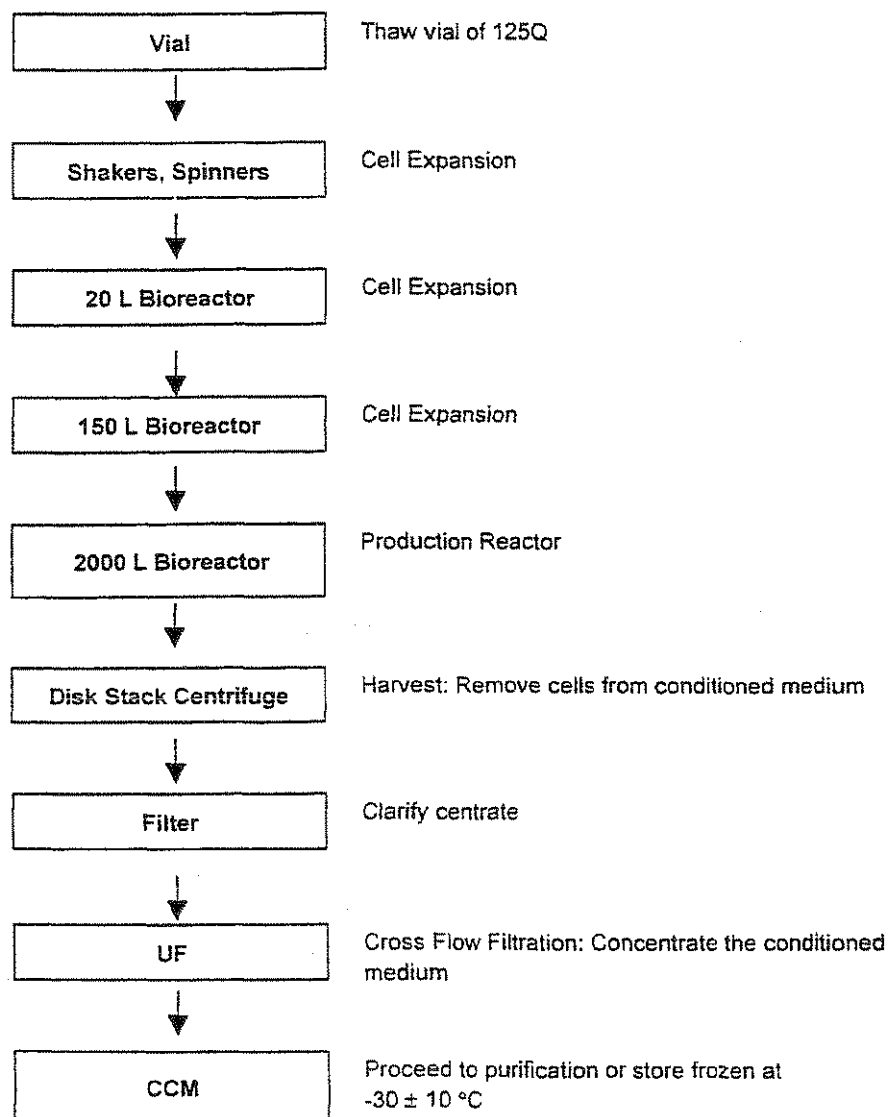


FIGURE 20

Mean Serum Calcium Percent Change From Baseline After Administering a
Single Dose of α OPGL-1 to Cynomolgus Monkeys

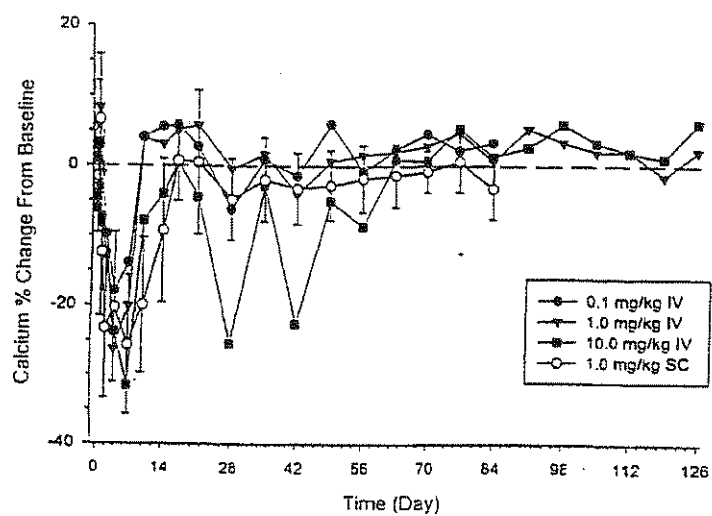


FIGURE 21

Mean Serum Alkaline Phosphatase Percent Change From Baseline After
Administering a Single Dose of α OPGL-1 to Cynomolgus Monkeys

