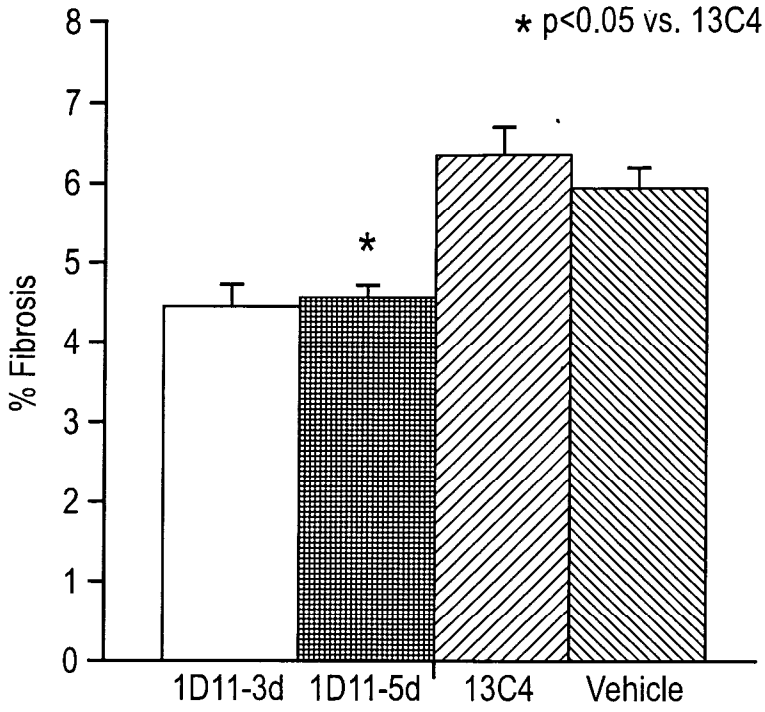

* p<0.05 vs. 13C4
% Fibrosis
8
7
6
5
4
3
2
1
0
*
1D11-3d
1D11-5d
13C4
Vehicle

FIG. 1

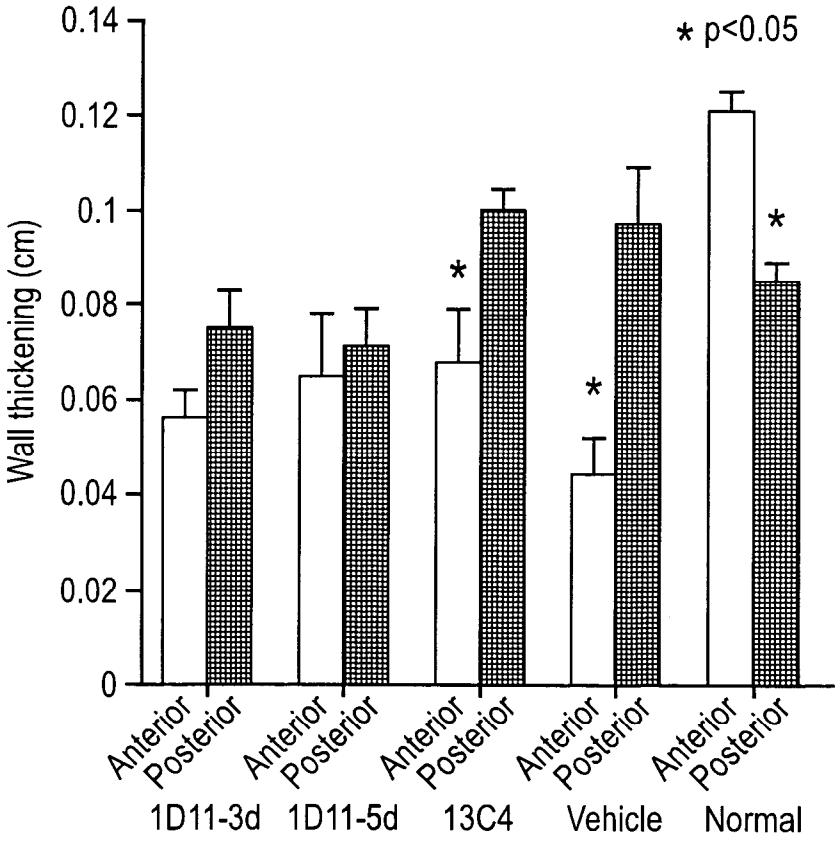

* p<0.05
Wall thickening (cm)
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
*
*
*
Anterior
Posterior
1D11-3d
1D11-5d
13C4
Vehicle
Normal

FIG. 2

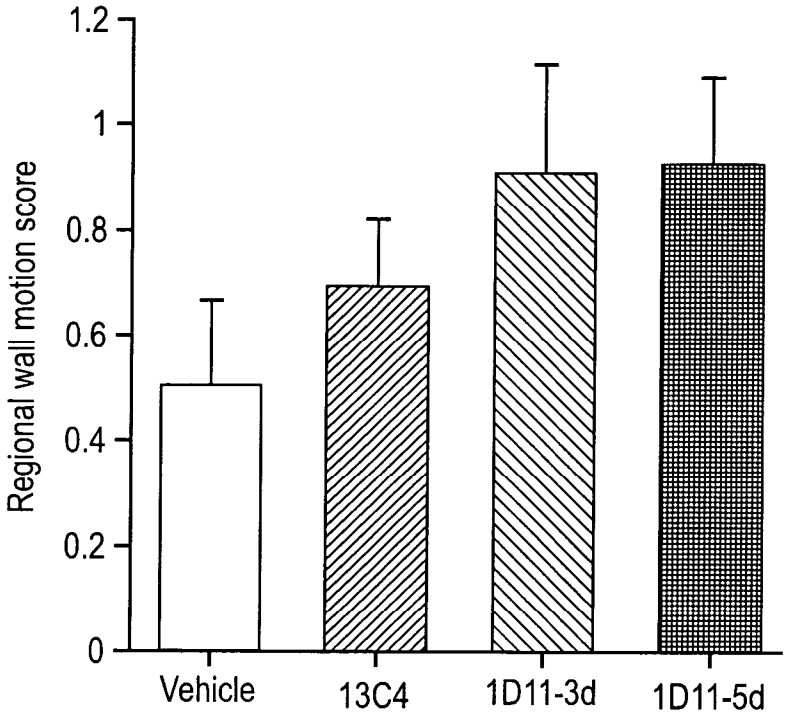

Regional wall motion score
1.2
1
0.8
0.6
0.4
0.2
0
Vehicle
13C4
1D11-3d
1D11-5d

FIG. 3

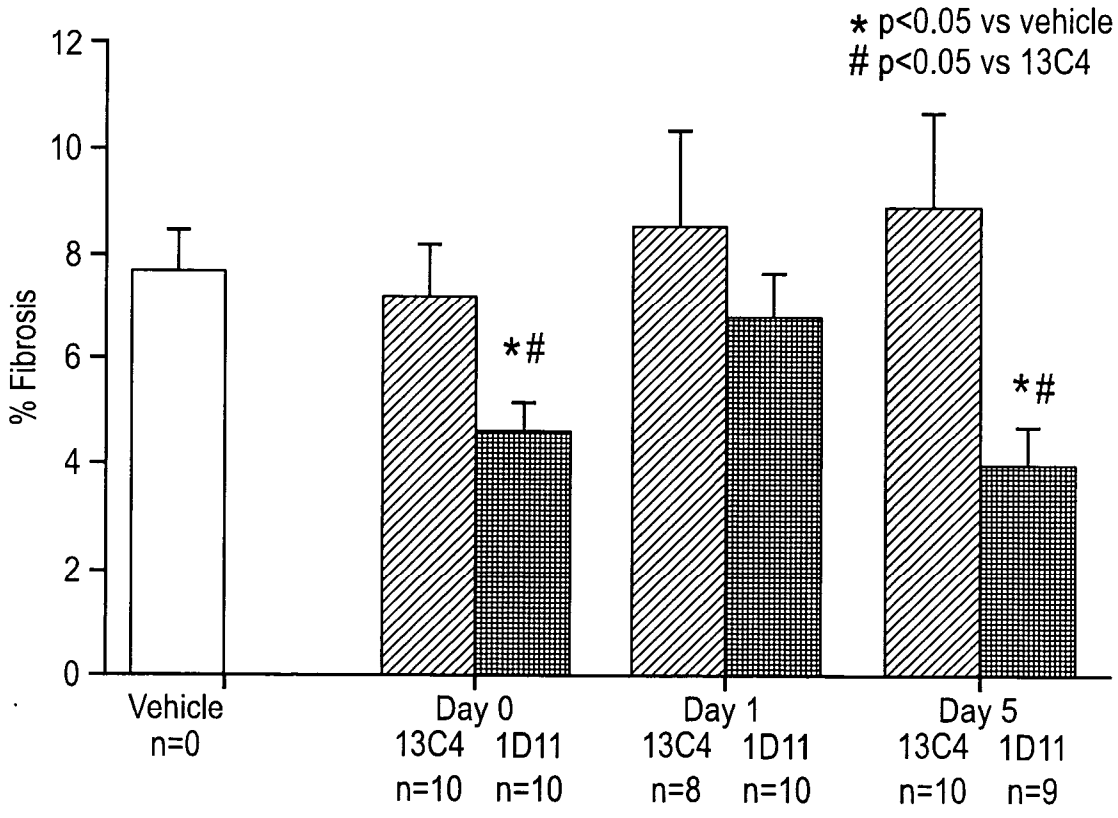
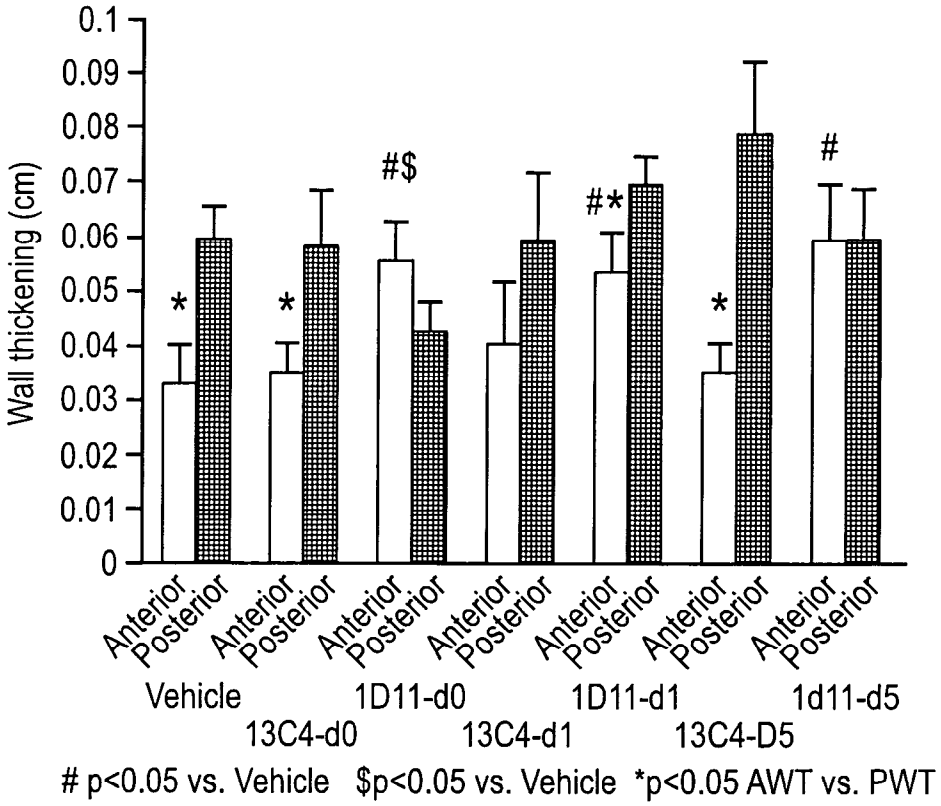

* p<0.05 vs vehicle
# p<0.05 vs 13C4
% Fibrosis
12
10
8
6
4
2
0
*#
*#
Vehicle
n=0
Day 0
13C4 1D11
n=10 n=10
Day 1
13C4 1D11
n=8 n=10
Day 5
13C4 1D11
n=10 n=9

FIG. 4



# p<0.05 vs. Vehicle $p<0.05 vs. Vehicle *p<0.05 AWT vs. PWT

FIG. 5

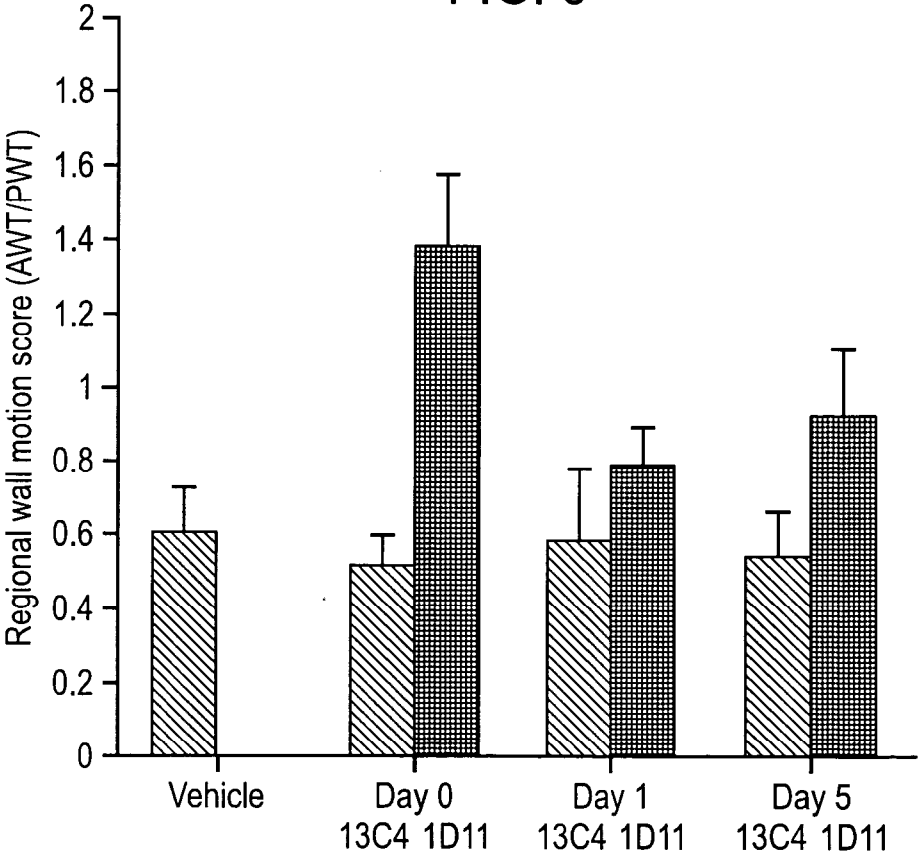


FIG. 6

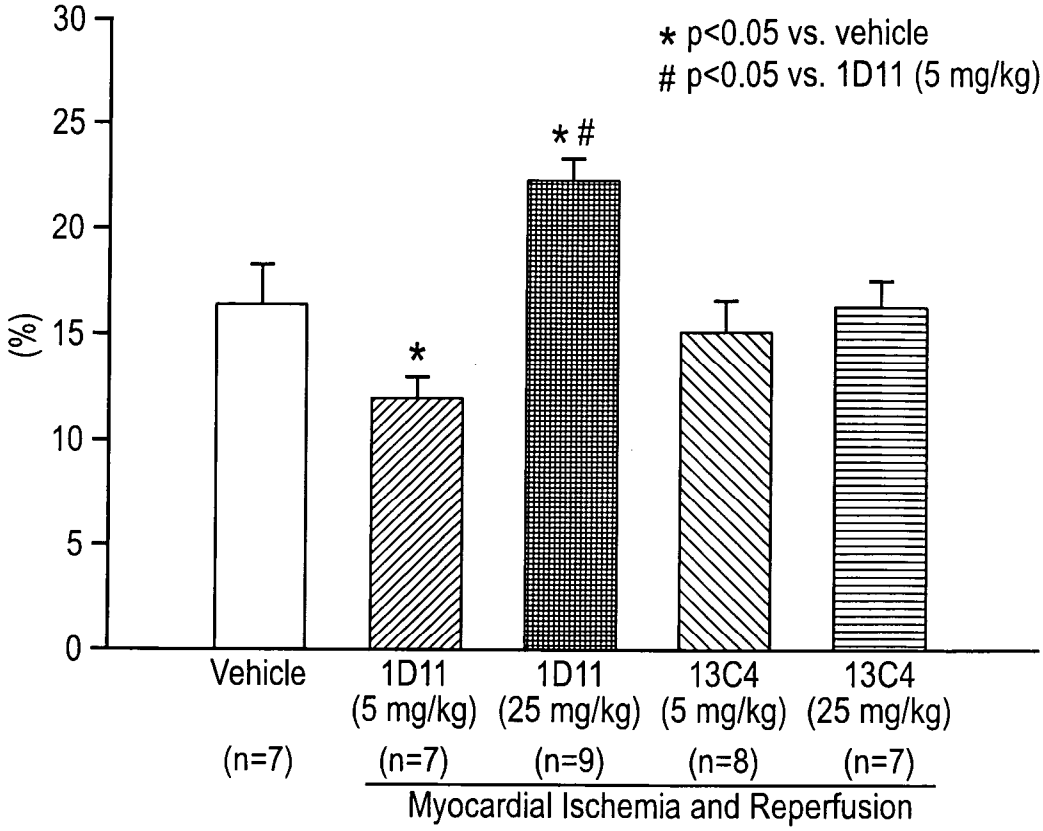

* p<0.05 vs. vehicle
# p<0.05 vs. 1D11 (5 mg/kg)
30
25
20
15
10
5
0
(%)
*
*#
Vehicle
1D11 (5 mg/kg)
1D11 (25 mg/kg)
13C4 (5 mg/kg)
13C4 (25 mg/kg)
(n=7)
(n=7)
(n=9)
(n=8)
(n=7)
Myocardial Ischemia and Reperfusion

FIG. 7

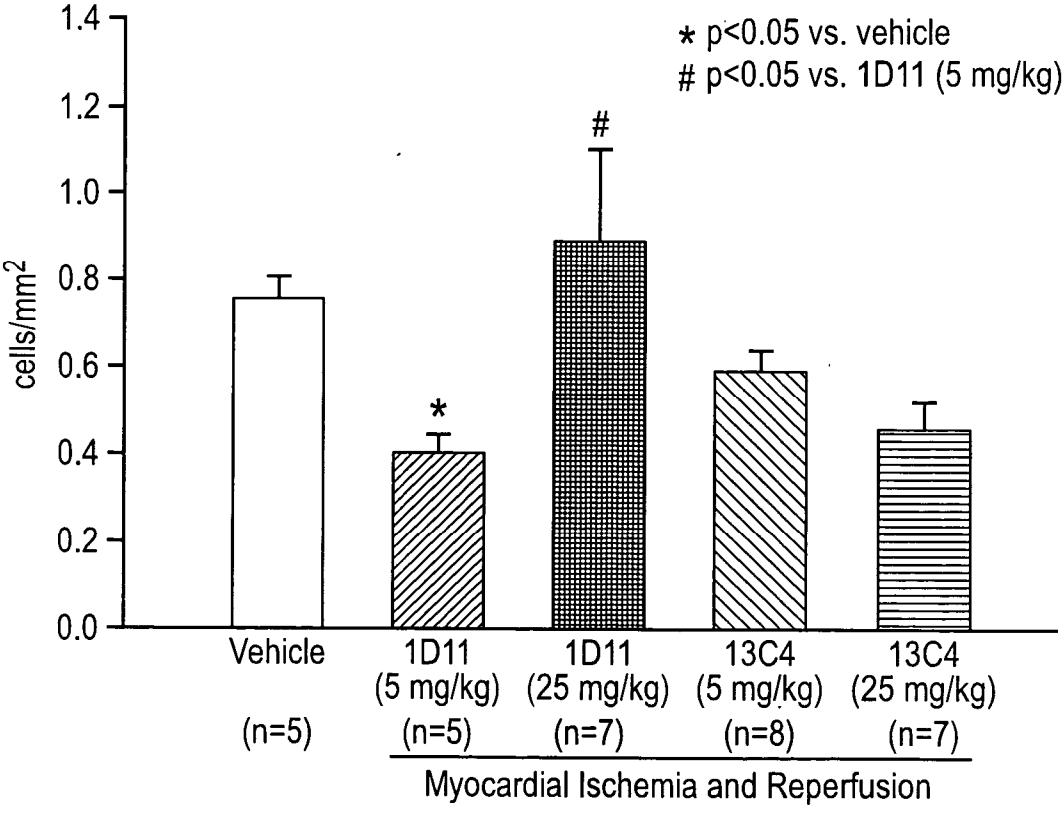

* p<0.05 vs. vehicle
# p<0.05 vs. 1D11 (5 mg/kg)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
cells/mm2
*
#
Vehicle
1D11 (5 mg/kg)
1D11 (25 mg/kg)
13C4 (5 mg/kg)
13C4 (25 mg/kg)
(n=5)
(n=5)
(n=7)
(n=8)
(n=7)
Myocardial Ischemia and Reperfusion

FIG. 8

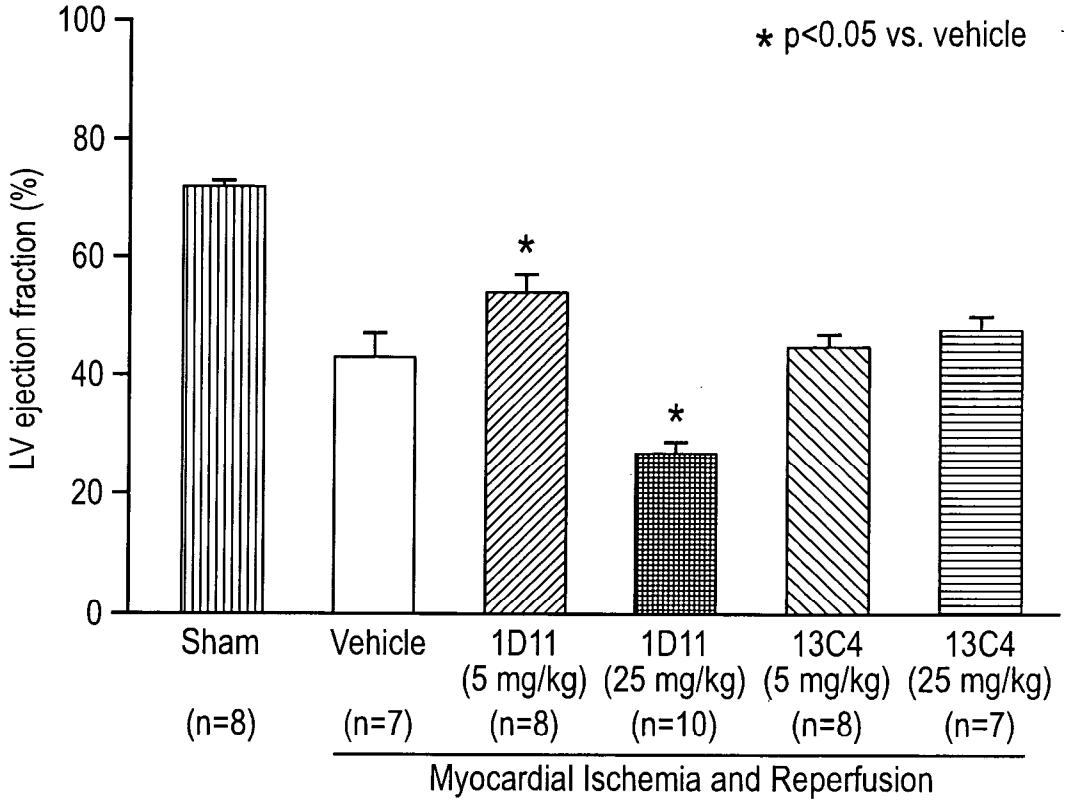

* p<0.05 vs. vehicle
LV ejection fraction (%)
100
80
60
40
20
0
*
*
Sham
(n=8)
Vehicle
(n=7)
1D11
(5 mg/kg)
(n=8)
1D11
(25 mg/kg)
(n=10)
13C4
(5 mg/kg)
(n=8)
13C4
(25 mg/kg)
(n=7)
Myocardial Ischemia and Reperfusion

FIG. 9

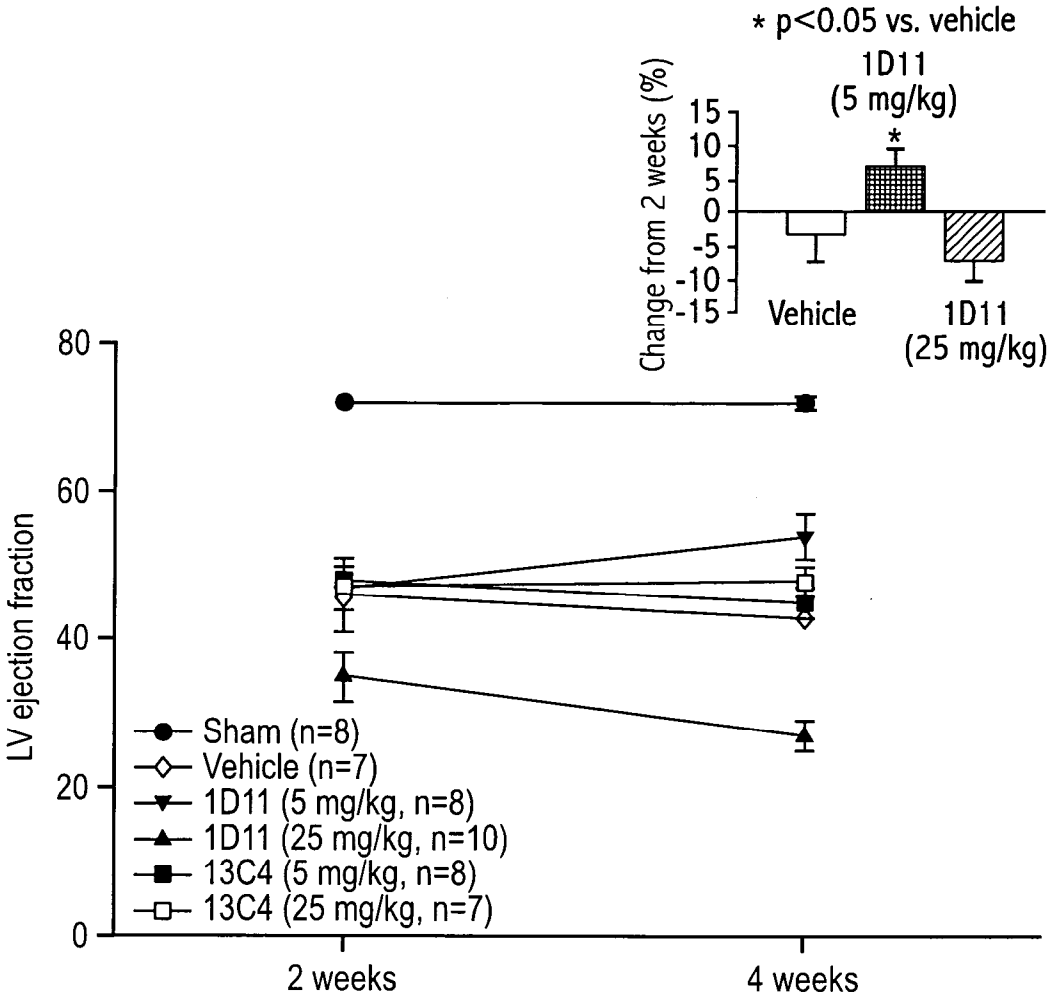

* p<0.05 vs. vehicle
1D11
(5 mg/kg)
*
Change from 2 weeks (%)
15
10
5
0
-5
-10
-15
Vehicle
1D11
(25 mg/kg)
80
60
40
20
0
LV ejection fraction
Sham (n=8)
Vehicle (n=7)
1D11 (5 mg/kg, n=8)
1D11 (25 mg/kg, n=10)
13C4 (5 mg/kg, n=8)
13C4 (25 mg/kg, n=7)
2 weeks
4 weeks

FIG. 10

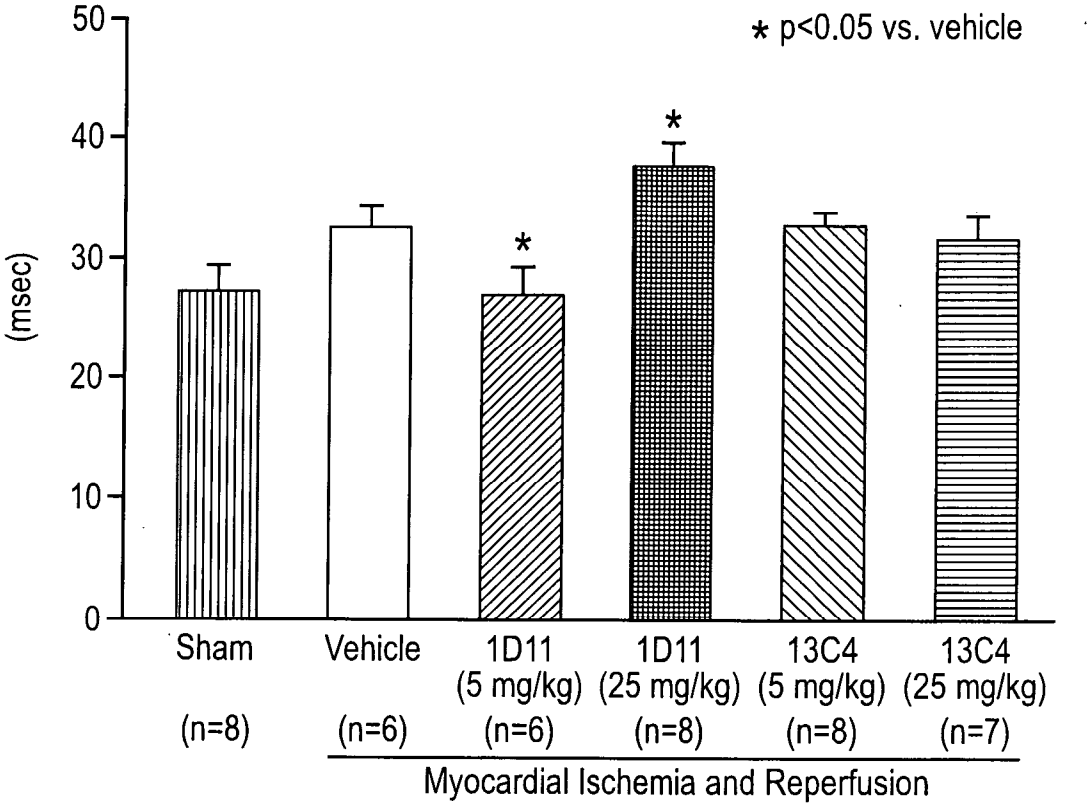

* p<0.05 vs. vehicle
(msec)
50
40
30
20
10
0
Sham
Vehicle
1D11 (5 mg/kg)
1D11 (25 mg/kg)
13C4 (5 mg/kg)
13C4 (25 mg/kg)
(n=8)
(n=6)
(n=6)
(n=8)
(n=8)
(n=7)
Myocardial Ischemia and Reperfusion

FIG. 11

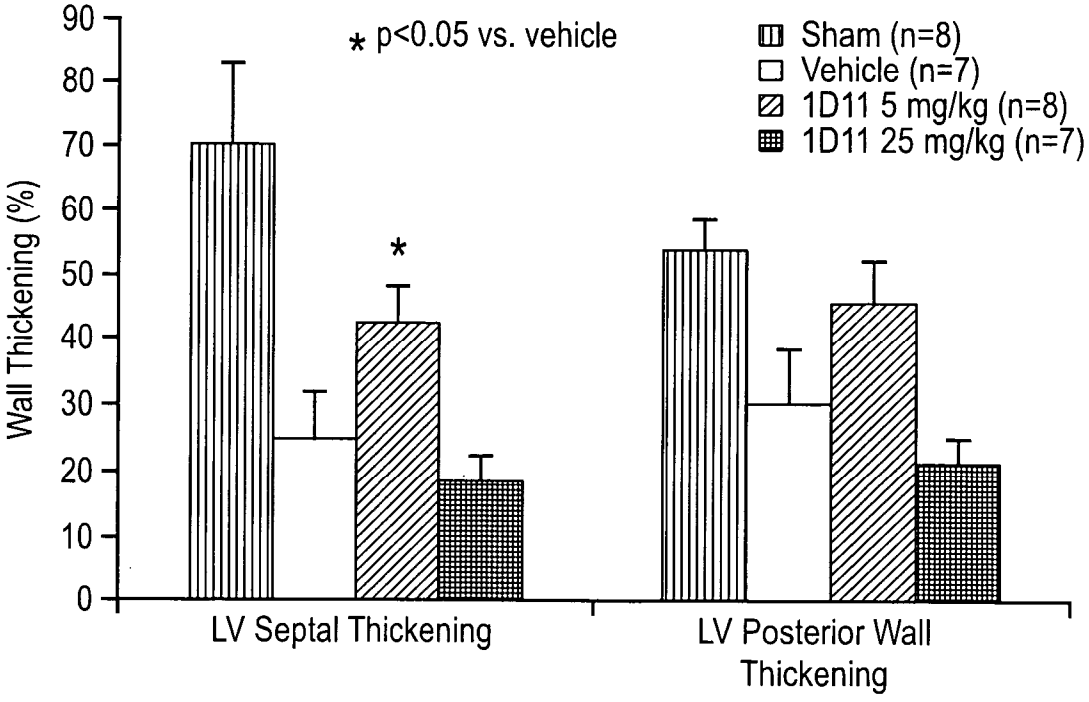

* p<0.05 vs. vehicle
Sham (n=8)
Vehicle (n=7)
1D11 5 mg/kg (n=8)
1D11 25 mg/kg (n=7)
Wall Thickening (%)
90
80
70
60
50
40
30
20
10
0
LV Septal Thickening
LV Posterior Wall Thickening

FIG. 12

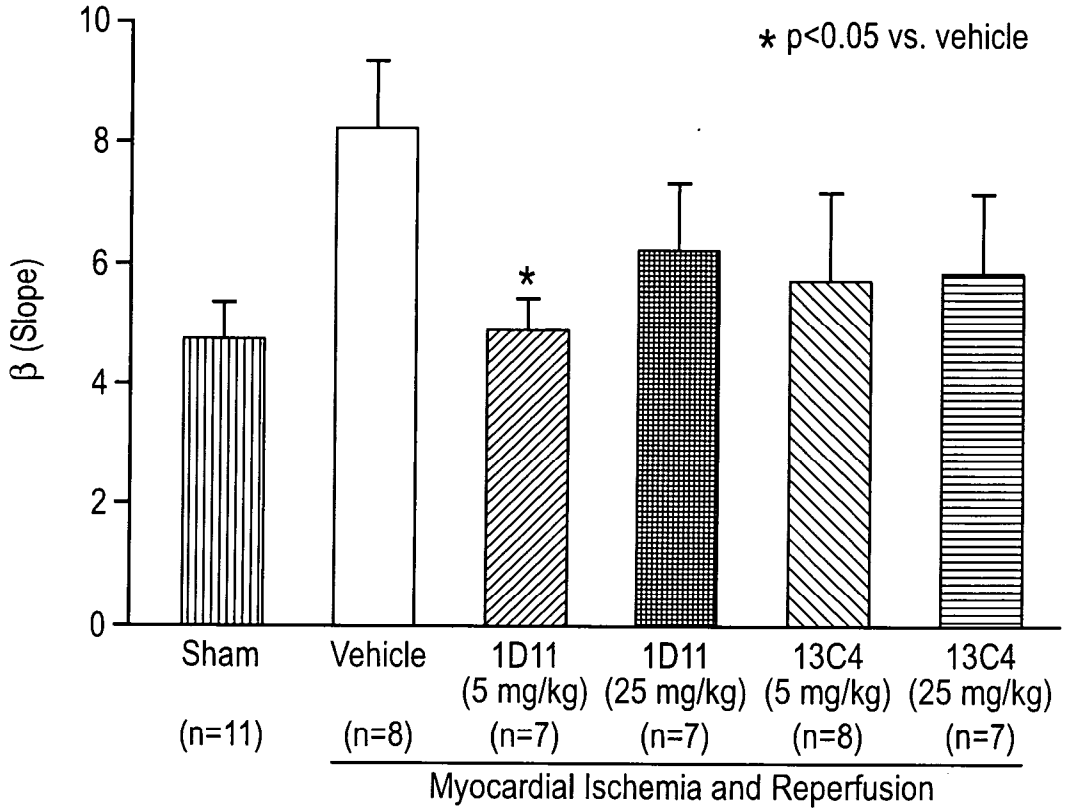

* p<0.05 vs. vehicle
β (Slope)
10
8
6
4
2
0
*
Sham
(n=11)
Vehicle
(n=8)
1D11
(5 mg/kg)
(n=7)
1D11
(25 mg/kg)
(n=7)
13C4
(5 mg/kg)
(n=8)
13C4
(25 mg/kg)
(n=7)
Myocardial Ischemia and Reperfusion

FIG. 13

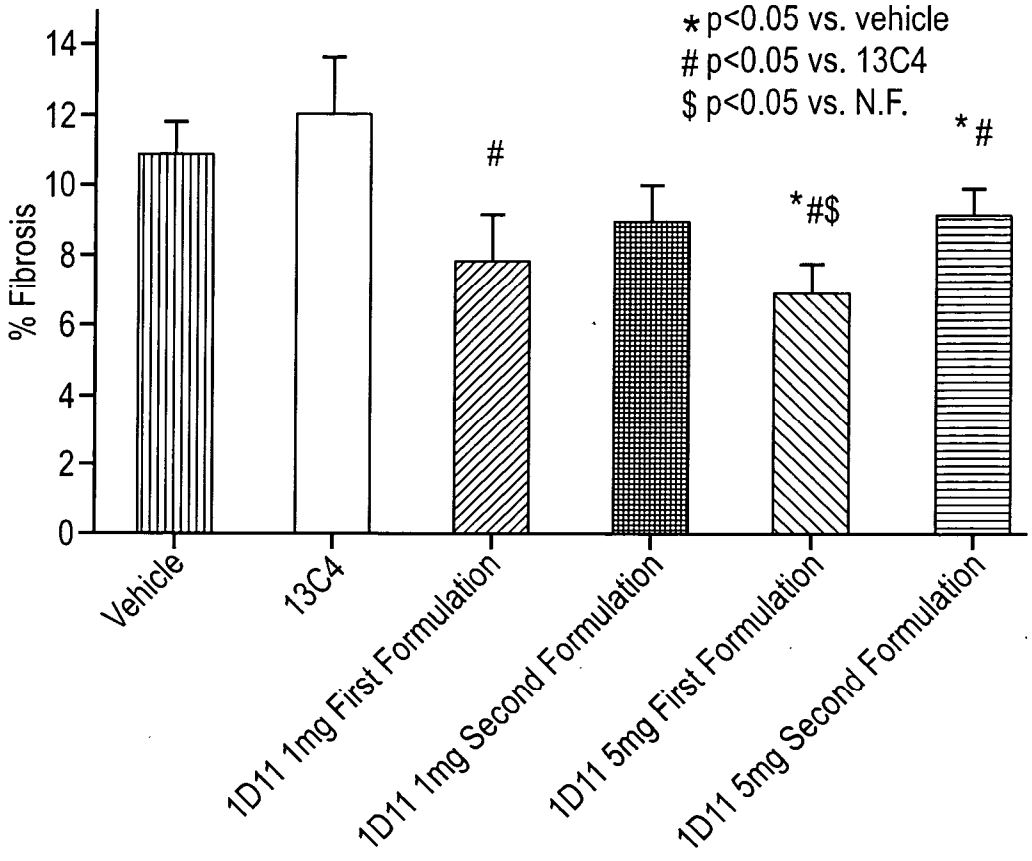

* p<0.05 vs. vehicle
# p<0.05 vs. 13C4
$ p<0.05 vs. N.F.
% Fibrosis
0
2
4
6
8
10
12
14
#
*#$
*#
Vehicle
13C4
1D11 1mg First Formulation
1D11 1mg Second Formulation
1D11 5mg First Formulation
1D11 5mg Second Formulation

FIG. 14

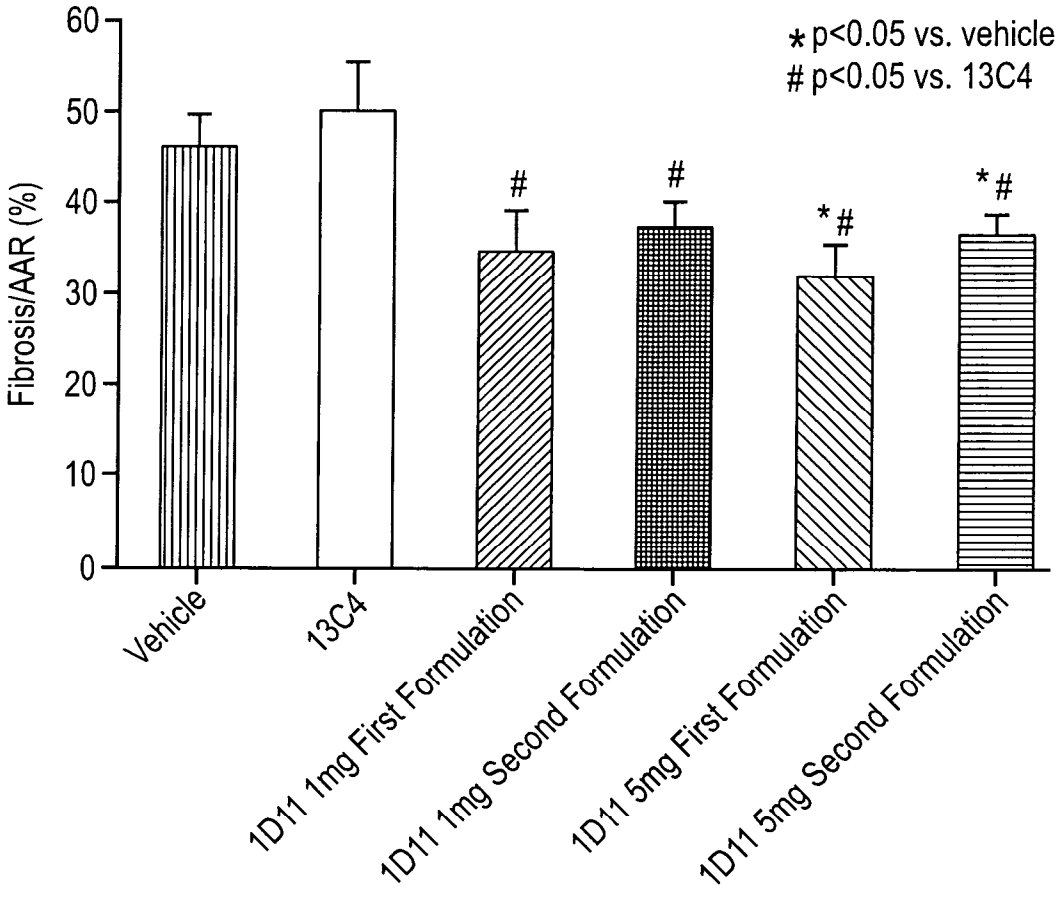

* p<0.05 vs. vehicle
# p<0.05 vs. 13C4
Fibrosis/AAR (%)
60
50
40
30
20
10
0
#
#
*#
*#
Vehicle
13C4
1D11 1mg First Formulation
1D11 1mg Second Formulation
1D11 5mg First Formulation
1D11 5mg Second Formulation

FIG. 15

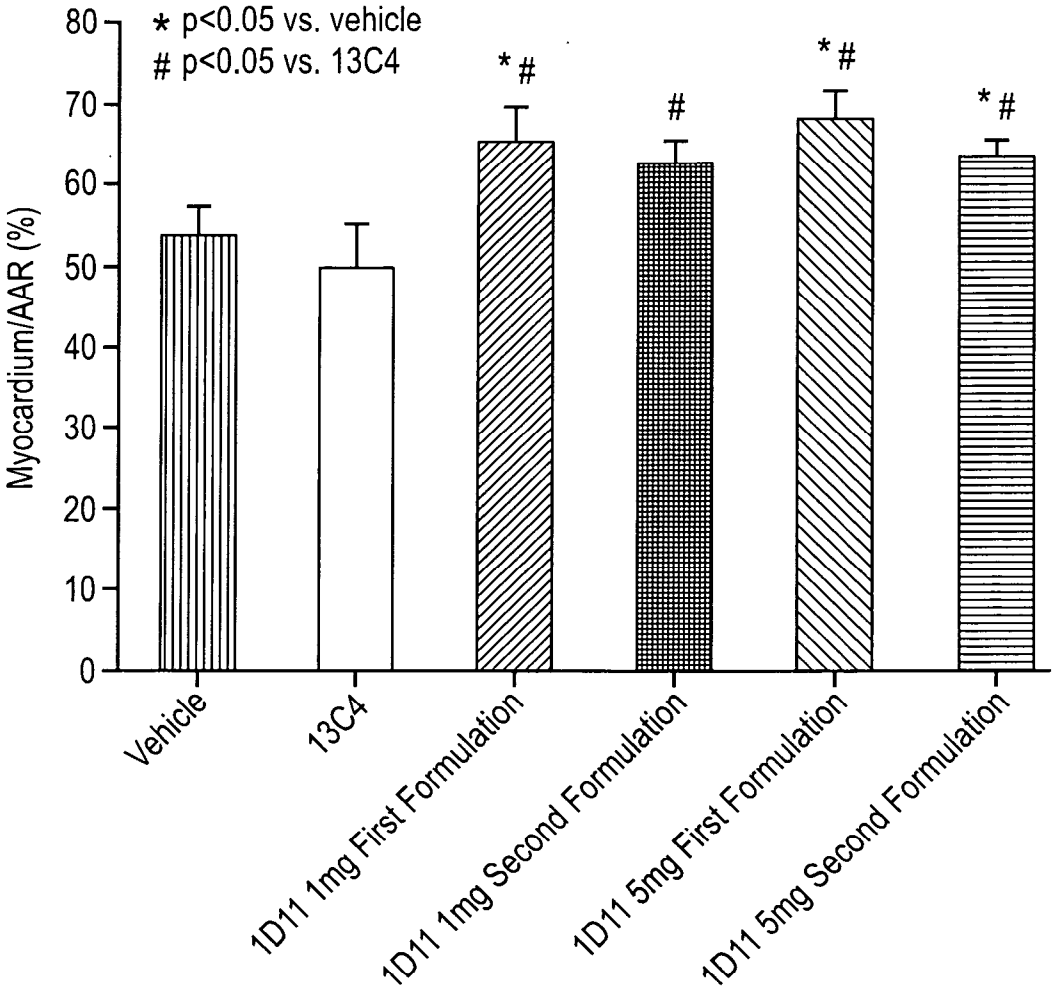

* p<0.05 vs. vehicle
# p<0.05 vs. 13C4
Myocardium/AAR (%)
80
70
60
50
40
30
20
10
0
*#
#
*#
*#
Vehicle
13C4
1D11 1mg First Formulation
1D11 1mg Second Formulation
1D11 5mg First Formulation
1D11 5mg Second Formulation

FIG. 16

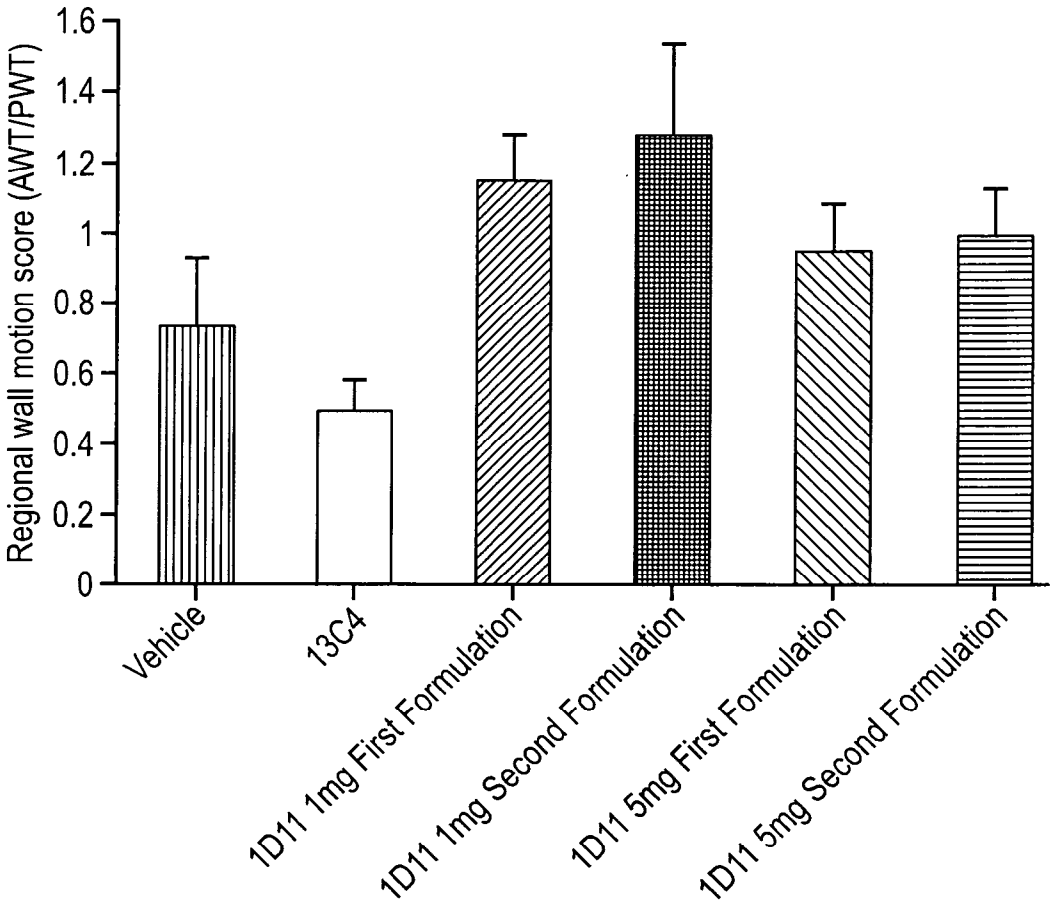

Regional wall motion score (AWT/PWT)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Vehicle
13C4
1D11 1mg First Formulation
1D11 1mg Second Formulation
1D11 5mg First Formulation
1D11 5mg Second Formulation

FIG. 17

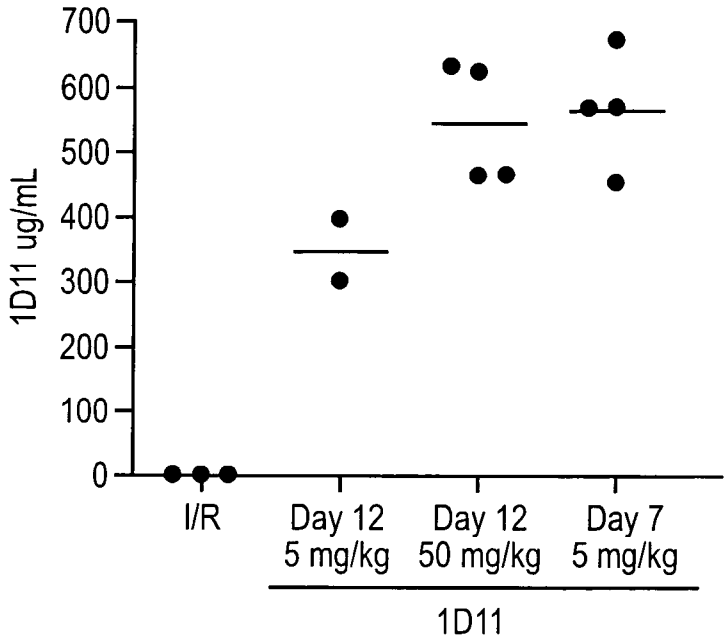

700
600
500
400
300
200
100
0
1D11 ug/mL
I/R
Day 12
5 mg/kg
Day 12
50 mg/kg
Day 7
5 mg/kg
1D11

FIG. 18

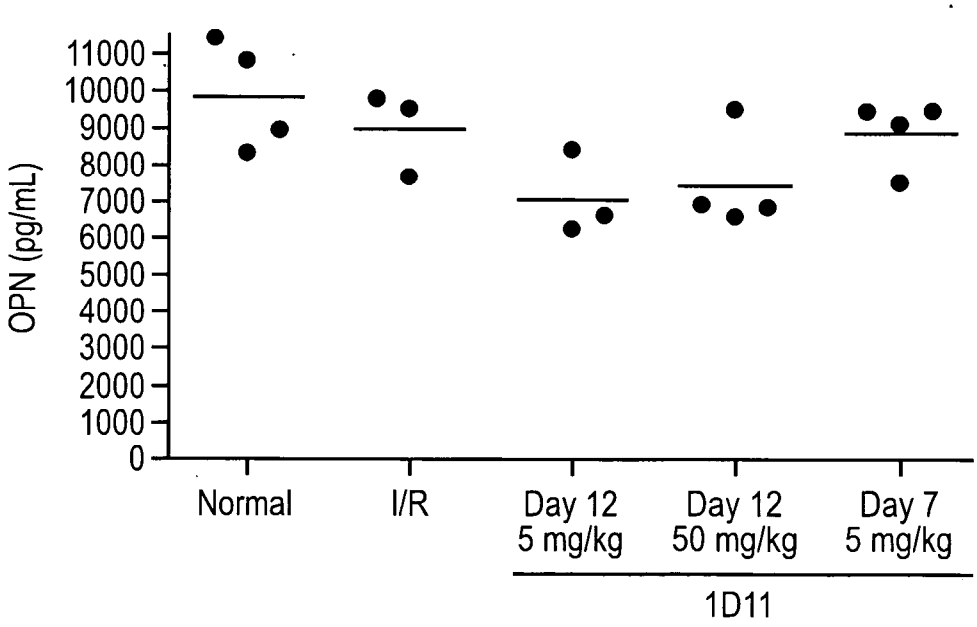

11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
OPN (pg/mL)
Normal
I/R
Day 12
5 mg/kg
Day 12
50 mg/kg
Day 7
5 mg/kg
1D11

FIG. 19

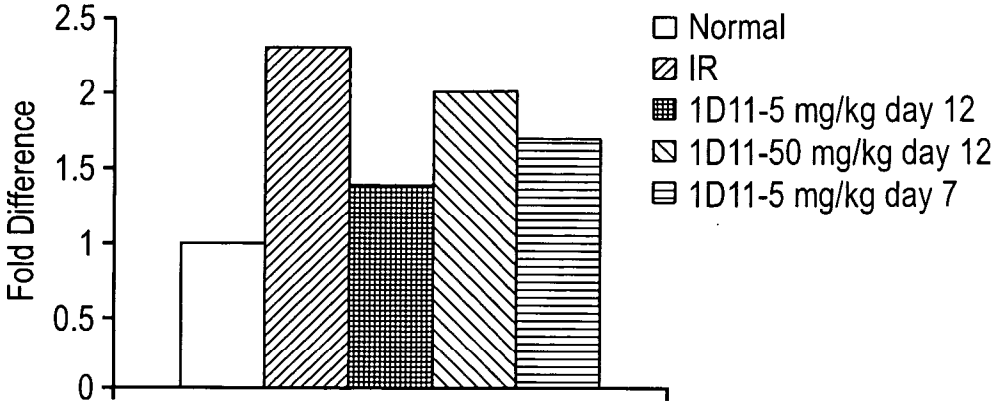


FIG. 20

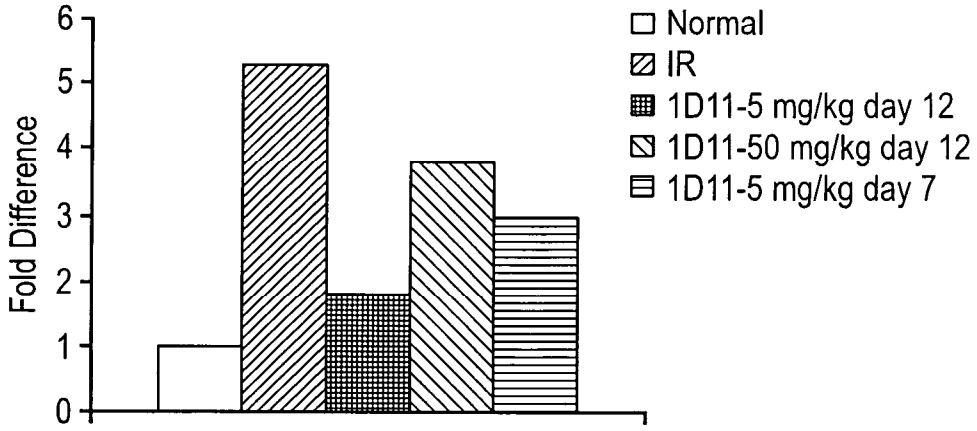


FIG. 21

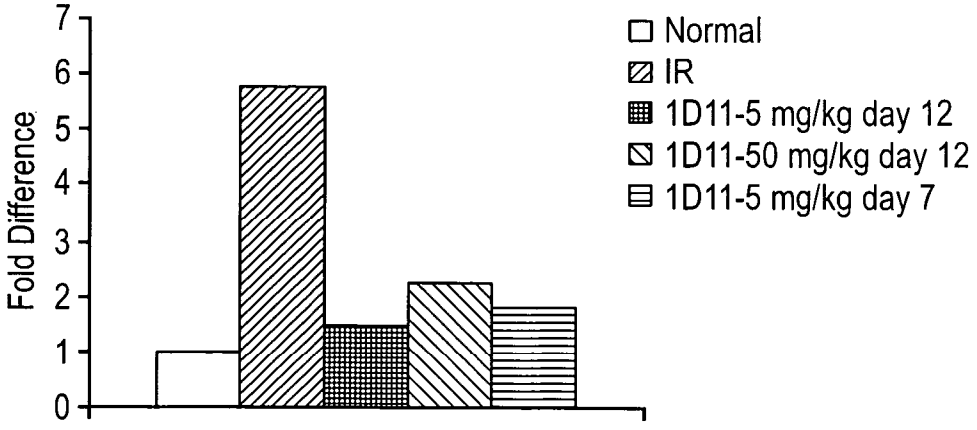


FIG. 22

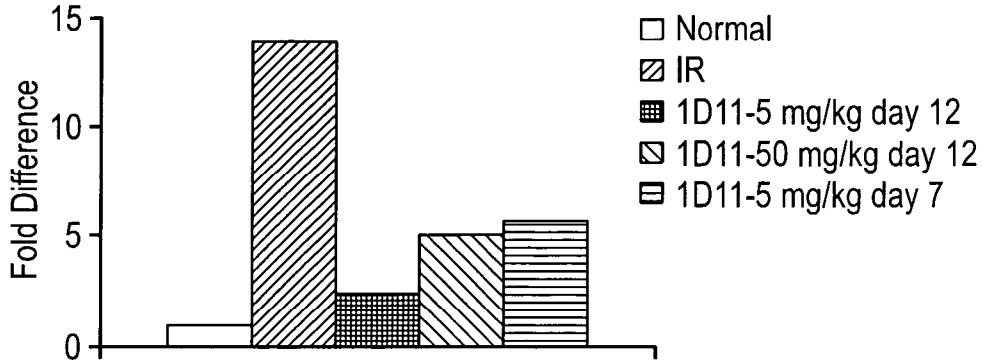


FIG. 23

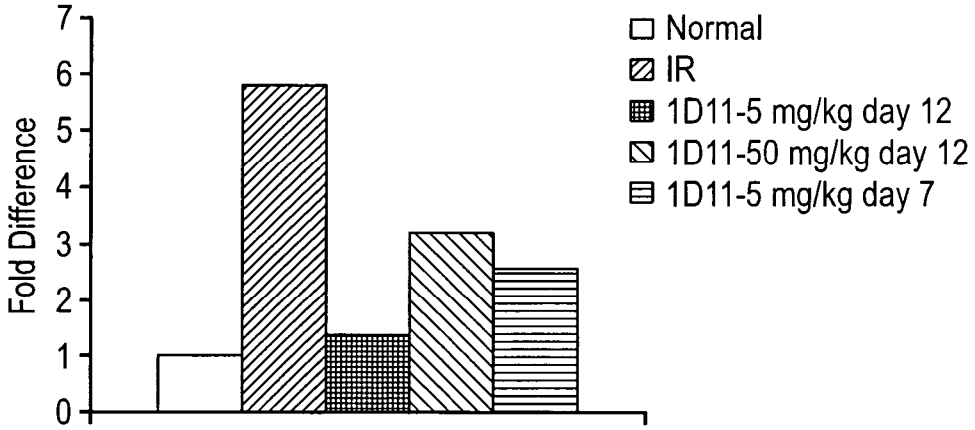


FIG. 24

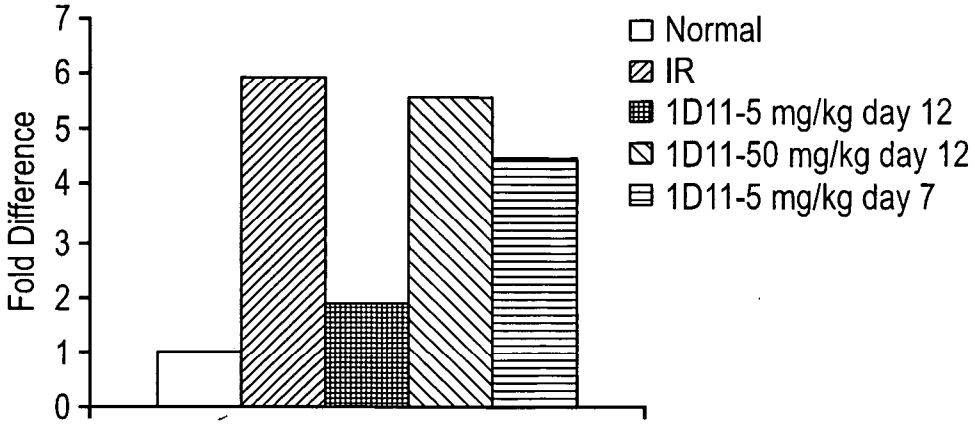


FIG. 25

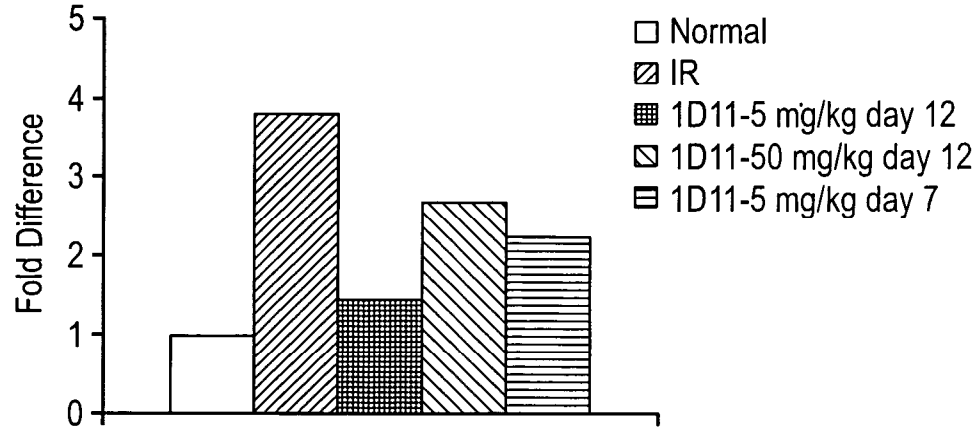


FIG. 26

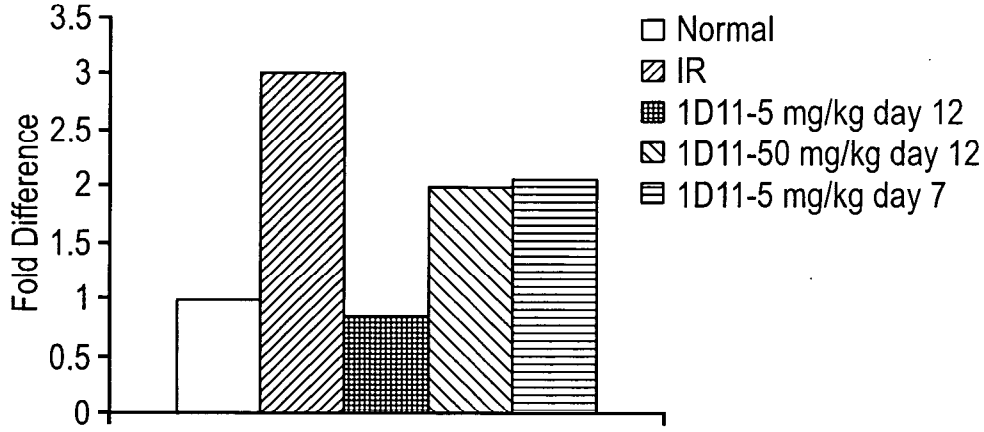


FIG. 27

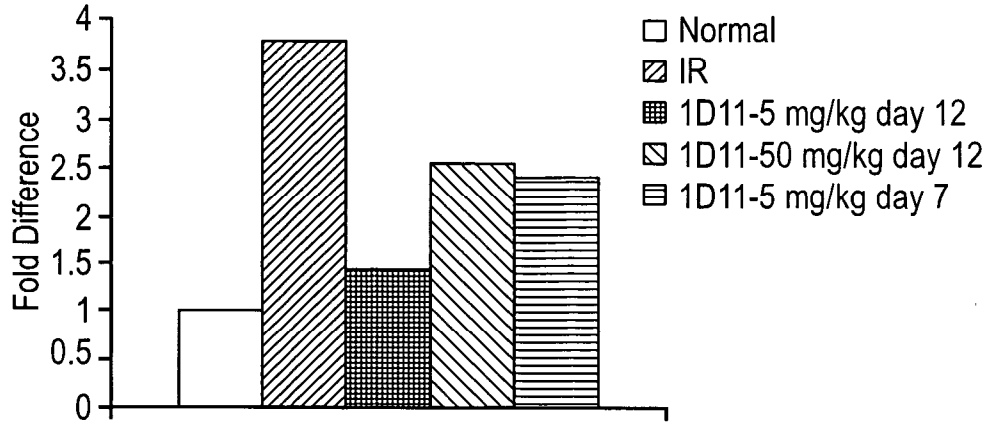


FIG. 28

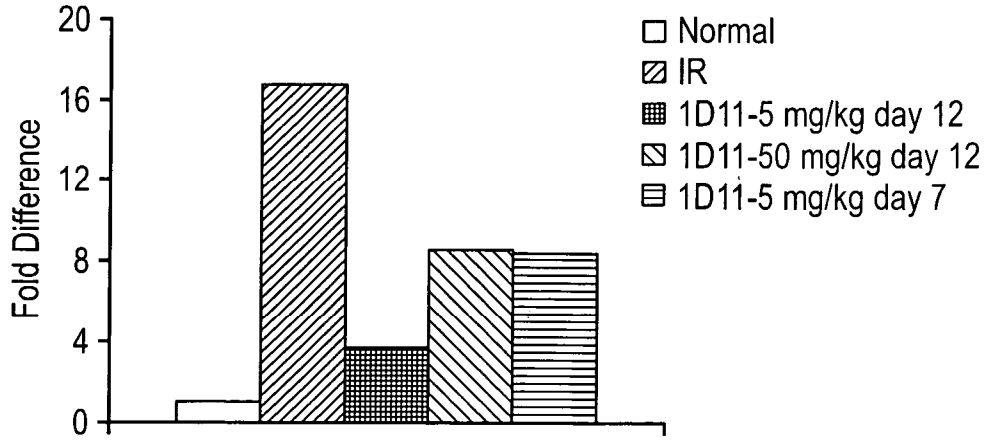

Fold Difference
20
16
12
8
4
0
Normal
IR
1D11-5 mg/kg day 12
1D11-50 mg/kg day 12
1D11-5 mg/kg day 7

FIG. 29

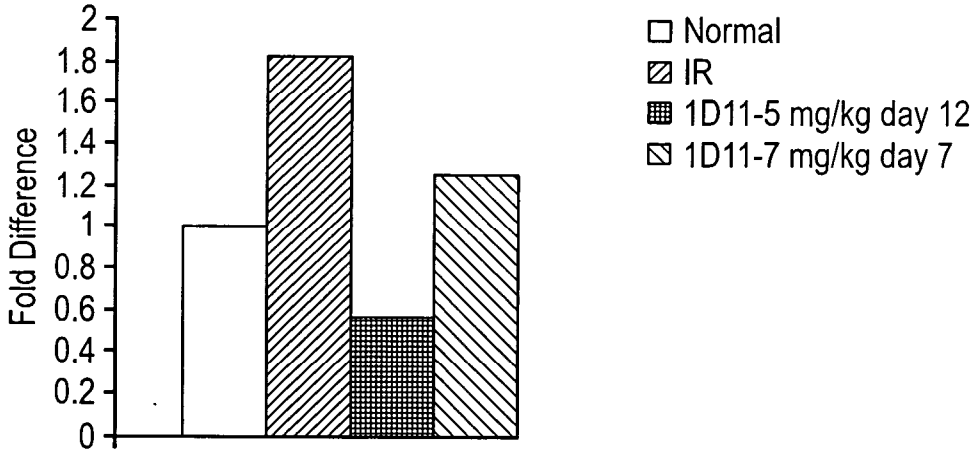

Fold Difference
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Normal
IR
1D11-5 mg/kg day 12
1D11-7 mg/kg day 7

FIG. 30

<110> Akita, Geoff
Lonning, Scott
Gregory, Richard
Kudej, Amelia

<120> TREATMENT OF MYOCARDIAL INFARCTION USING TGF-B ANTAGONISTS

<130> 0076524-000003

<140> Unassigned
<141> 2011-09-01

<150> US 61/379,315
<151> 2010-09-01

<160> 31

<210> 1
<211> 360
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1073G12 VH

<400> 1
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60
tcctgcaagg cttctggata caccttcagt agcaatgtta tcagctgggt gcgccaggcc 120
cctggacaag ggctcgagtg gatgggggg gtcatcccta ttgttgatat tgcgaactac 180
gcacagagat tcaagggcag agtcacgatt accgcggacg aatccactag tacaacttac 240
atggagttga gcagcctgag gtctgaggac acggccgtgt attactgtgc gagcacactt 300
ggtctcgtcc tggatgctat ggactactgg ggtcagggta cgttggtcac cgtctcctca 360

<210> 2
<211> 120
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 VH

<400> 2
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Ser Asn
20 25 30
Val Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe
50 55 60
Lys Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Thr Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Ser Thr Leu Gly Leu Val Leu Asp Ala Met Asp Tyr Trp Gly Gln
100 105 110
Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 3
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 HCDR1

<400> 3
Ser Asn Val Ile Ser

1 5

<210> 4
<211> 17
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 HCDR2

<400> 4
Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe Lys
1 5 10 15
Gly

<210> 5
<211> 11
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 HCDR3

<400> 5
Thr Leu Gly Leu Val Leu Asp Ala Met Asp Tyr
1 5 10

<210> 6
<211> 324
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1073G12 VL

<400> 6
gaaacggtac tcacgcagtc tccaggtacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtcttggc agcagctact tagcctggta tcagcagaaa 120
cctggtcagg ctcccaggct cctcatctat ggtgcatcca gcagggcacc tggcatccca 180
gacaggttca gtggcagtgg gtctggtacc gacttcactc tcaccatcag ccgactggag 240
cctgaagatt ttgcagttta ttactgtcag cagtatgctg actcaccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 7
<211> 108
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 VL

<400> 7
Glu Thr Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Gly Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Pro Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Asp Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 8
<211> 12

<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 LCDR1

<400> 8
Arg Ala Ser Gln Ser Leu Gly Ser Ser Tyr Leu Ala
1 5 10

<210> 9
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 LCDR2

<400> 9
Gly Ala Ser Ser Arg Ala Pro
1 5

<210> 10
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1073G12 LCDR3

<400> 10
Gln Gln Tyr Ala Asp Ser Pro Ile Thr
1 5

<210> 11
<211> 360
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1074B9 VH

<400> 11
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60
tcctgcaagg cttctggata caccttcagt agcaatgtta tcagctgggt gcgccaggcc 120
cctggacaag ggctcgagtg gatgggggg gtcatcccta ttgttgatat tgcgaactac 180
gcacagagat tcaagggcag agtcacgatt accgcggacg aatccactag tacaacttac 240
atggagttga gcagcctgag gtctgaggac acggccgtgt attactgtgc gctgccacgc 300
gctttcgtcc tggatgctat ggactactgg ggtcagggta cgttggtgac cgtctcctca 360

<210> 12
<211> 120
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 VH

<400> 12
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Ser Asn
20 25 30
Val Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe
50 55 60
Lys Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Thr Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Leu Pro Arg Ala Phe Val Leu Asp Ala Met Asp Tyr Trp Gly Gln
100 105 110
Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 13
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 HCDR1

<400> 13
Ser Asn Val Ile Ser
1 5

<210> 14
<211> 17
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 HCDR2

<400> 14
Gly Val Ile Pro Ile Val Asp Ile Ala Asn Tyr Ala Gln Arg Phe Lys
1 5 10 15
Gly

<210> 15
<211> 11
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 HCDR3

<400> 15
Pro Arg Ala Phe Val Leu Asp Ala Met Asp Tyr
1 5 10

<210> 16
<211> 324
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1074B9 VL

<400> 16
gaaacggtac tcacgcagtc tccaggtacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtcttggc agcagctact tagcctggta tcagcagaaa 120
cctggtcagg ctcccaggct cctcatctat ggtgcatcca gcagggcacc tggcatccca 180
gacaggttca gtggcagtgg gtctggtacc gacttcactc tcaccatcag ccgactggag 240
cctgaagatt ttgcagttta ttactgtcag cagtatgctg actcaccgat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 17
<211> 108
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 VL

<400> 17

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Glu Thr Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Gly Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Ala Ser Ser Arg Ala Pro Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Asp Ser Pro
                85                  90                  95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105
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<210> 18
<211> 12
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 LCDR1

<400> 18
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Arg Ala Ser Gln Ser Leu Gly Ser Ser Tyr Leu Ala
1               5                  10
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<210> 19
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 LCDR2

<400> 19
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Gly Ala Ser Ser Arg Ala Pro
1               5
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<210> 20
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1074B9 LCDR3

<400> 20
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Gln Gln Tyr Ala Asp Ser Pro Ile Thr
1               5
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<210> 21
<211> 363
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1287A10 VH

<400> 21
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tcctgcaagg cttctggagg caccttcagc acctctttca tcaattgggt gcgacaggcc    120
cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttgatat aacaaactac    180
gcacagaaat ttcagagcag agtcactatt accgcggaca aatccacgag caccgcctac    240
atggagctga gcagcctgcg ctctgaggac acggctgtgt attactgcgc acgcggaaat    300
ggtaactacg ccctggatgc tatggactac tggggtcagg gtacgttggt caccgtctcc    360
tca                                                                  363
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<210> 22

<211> 121
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 VH

<400> 22
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Thr Ser
20 25 30
Phe Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Gly Ile Ile Pro Ile Phe Asp Ile Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Ser Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Asn Gly Asn Tyr Ala Leu Asp Ala Met Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 23
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 HCDR1

<400> 23
Thr Ser Phe Ile Asn
1 5

<210> 24
<211> 17
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 HCDR2

<400> 24
Gly Ile Ile Pro Ile Phe Asp Ile Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15
Ser

<210> 25
<211> 12
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 HCDR3

<400> 25
Gly Asn Gly Asn Tyr Ala Leu Asp Ala Met Asp Tyr
1 5 10

<210> 26
<211> 324
<212> DNA
<213> Artificial sequence

<220>
<223> Synthetic Nucleotide sequence encoding PET1287A10 VL

<400> 26
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccagtca gagtgttagc agcagctact ttgcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccct 180
gacagattca gtggcagcgg gtctgggaca gatttcactc tcaccatcag ccgcctggag 240
cctgaagatt tcgcagttta ttactgtcag caatattatg atagtcccat caccttcggc 300
caagggacac gactggagat taaa 324

<210> 27
<211> 108
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 VL

<400> 27
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Phe Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Asp Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 28
<211> 12
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 LCDR1

<400> 28
Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Phe Ala
1 5 10

<210> 29
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 LCDR2

<400> 29
Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 30
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Amino acid sequence of PET1287A10 LCDR3

<400> 30
Gln Gln Tyr Tyr Asp Ser Pro Ile Thr
1 5

<210> 31
<211> 11
<212> PRT
<213> Artificial sequence
<220>

<223> Synthetic Amino acid sequence of FR4
<400> 31
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10