

FIG.1



FIG.2



FIG.3



FIG.4

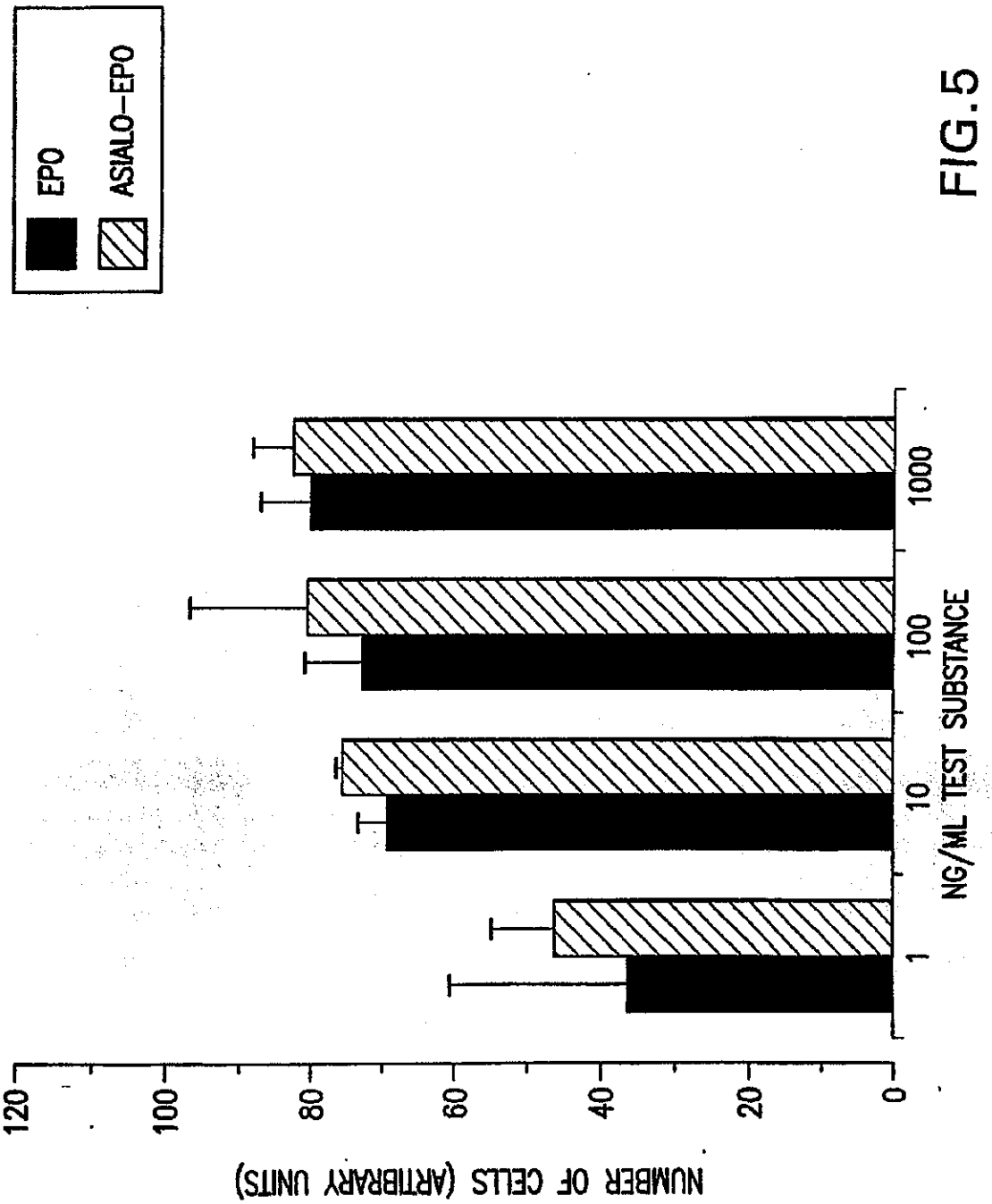

EPO
ASIALO-EPO
NUMBER OF CELLS (ARTIBRARY UNITS)
0
20
40
60
80
100
120
1
10
100
1000
NG/ML TEST SUBSTANCE

FIG.5

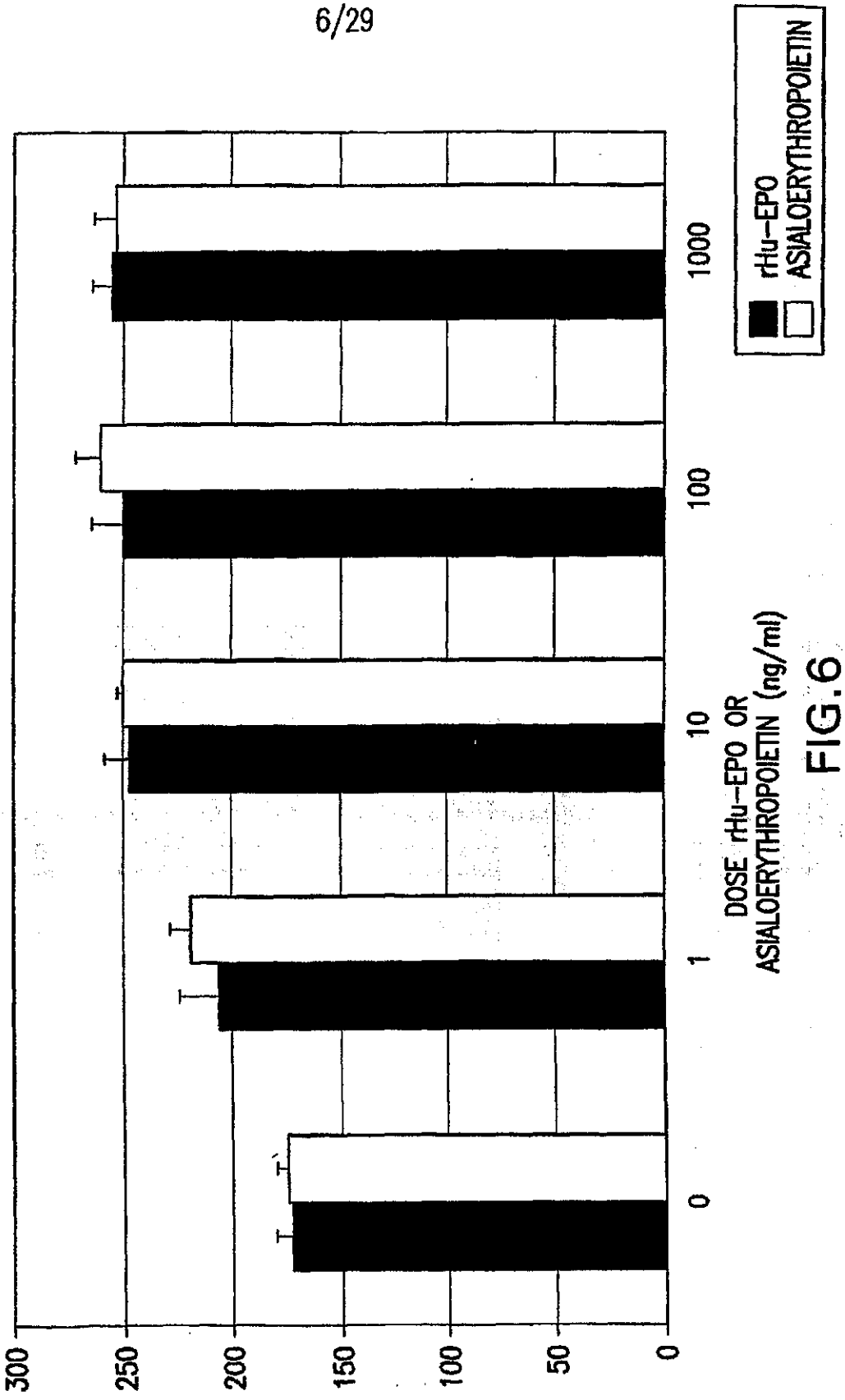
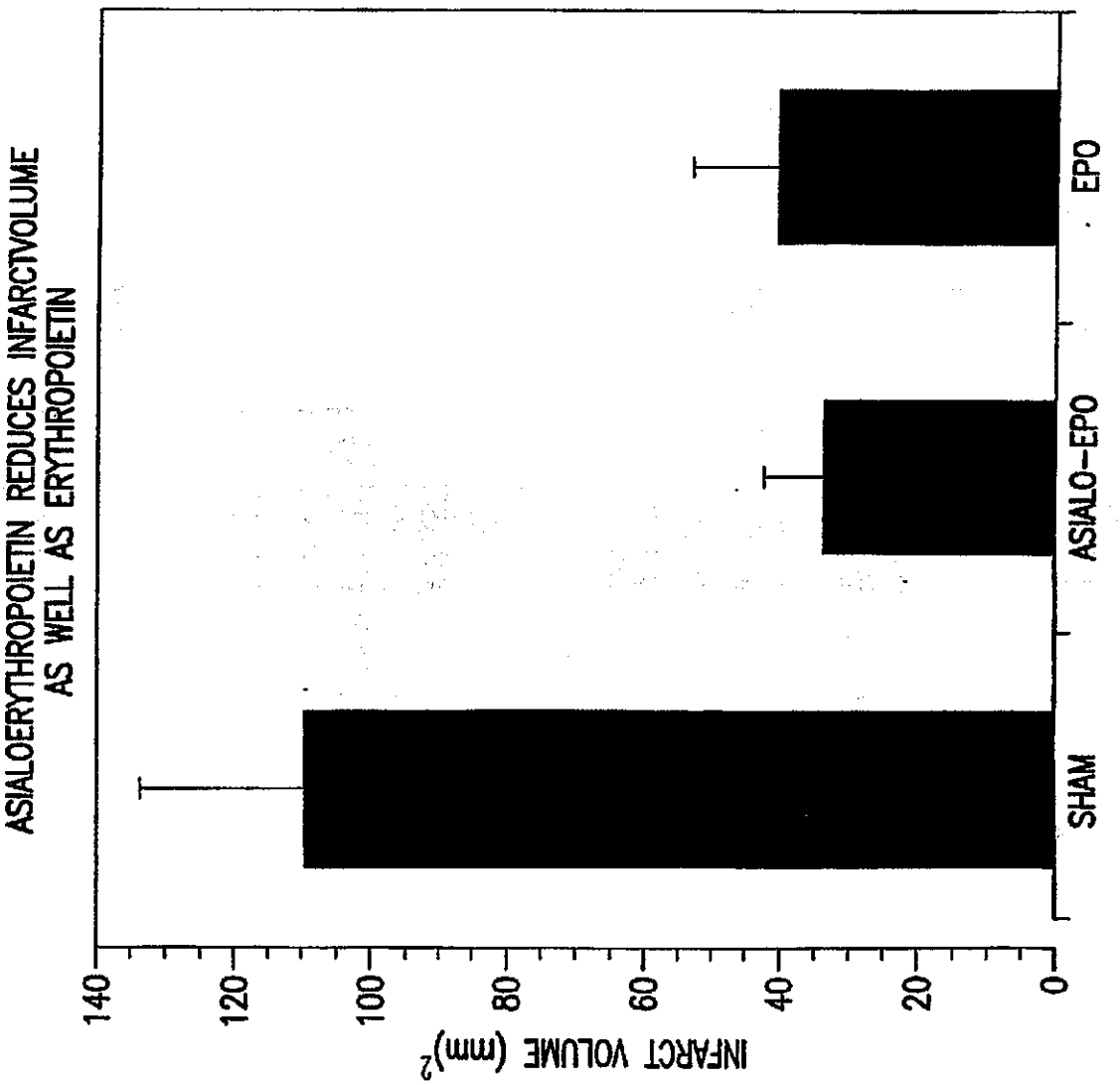

rHu-EPO
ASIALOERYTHROPOIETIN
300
250
200
150
100
50
0
0
1
10
100
1000
DOSE rHu-EPO OR
ASIALOERYTHROPOIETIN (ng/ml)

FIG.6

FIG. 7


ASIALOERYTHROPOIETIN REDUCES INFARCTVOLUME AS WELL AS ERYTHROPOIETIN
INFARCT VOLUME (mm)²
0
20
40
60
80
100
120
140
SHAM
ASIALO-EPO
EPO

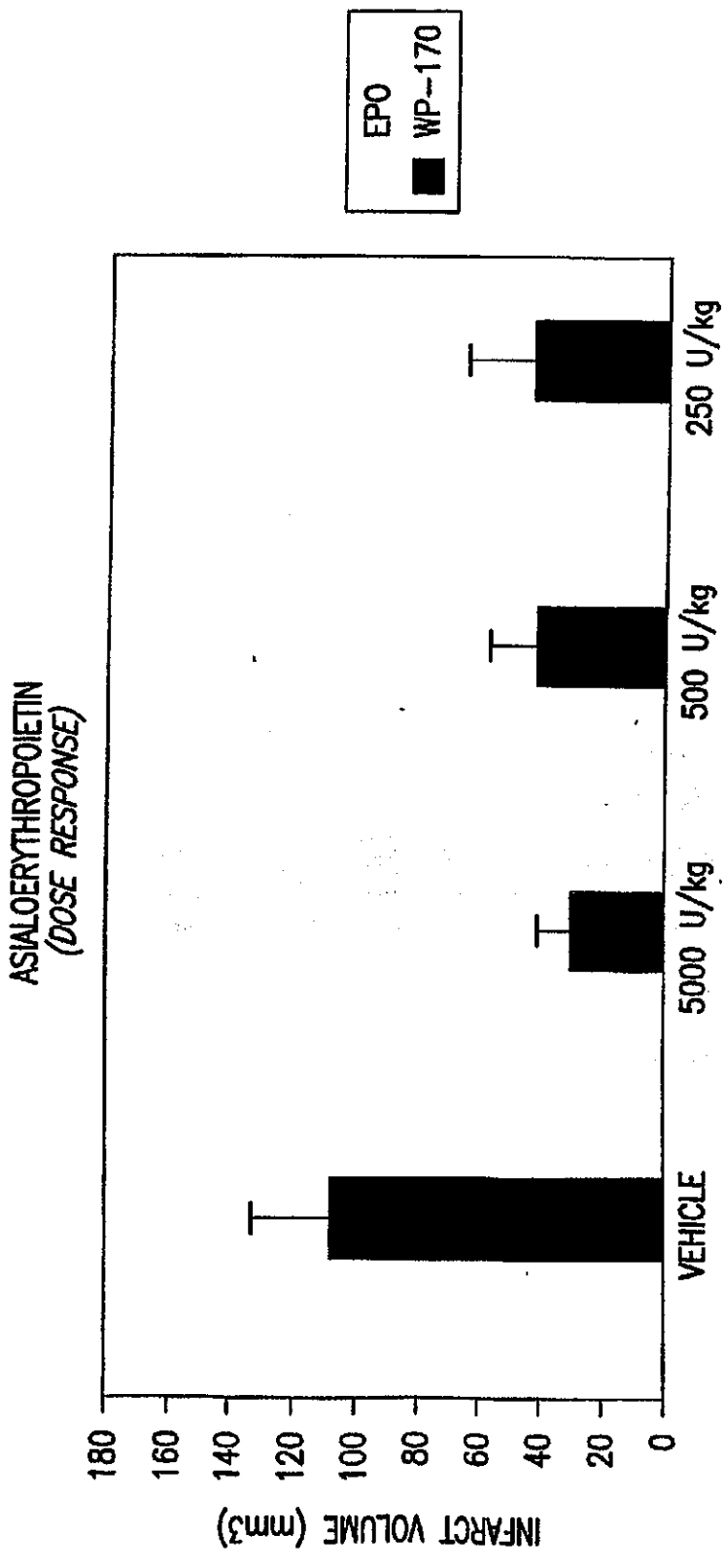

EPO
WP-170
ASIALOERYTHROPOIETIN
(DOSE RESPONSE)
INFARCT VOLUME (mm3)
180
160
140
120
100
80
60
40
20
0
VEHICLE
5000 U/kg
500 U/kg
250 U/kg
n FOR EACH GROUP IS GREATER
THAN OR EQUAL TO 4

FIG.8

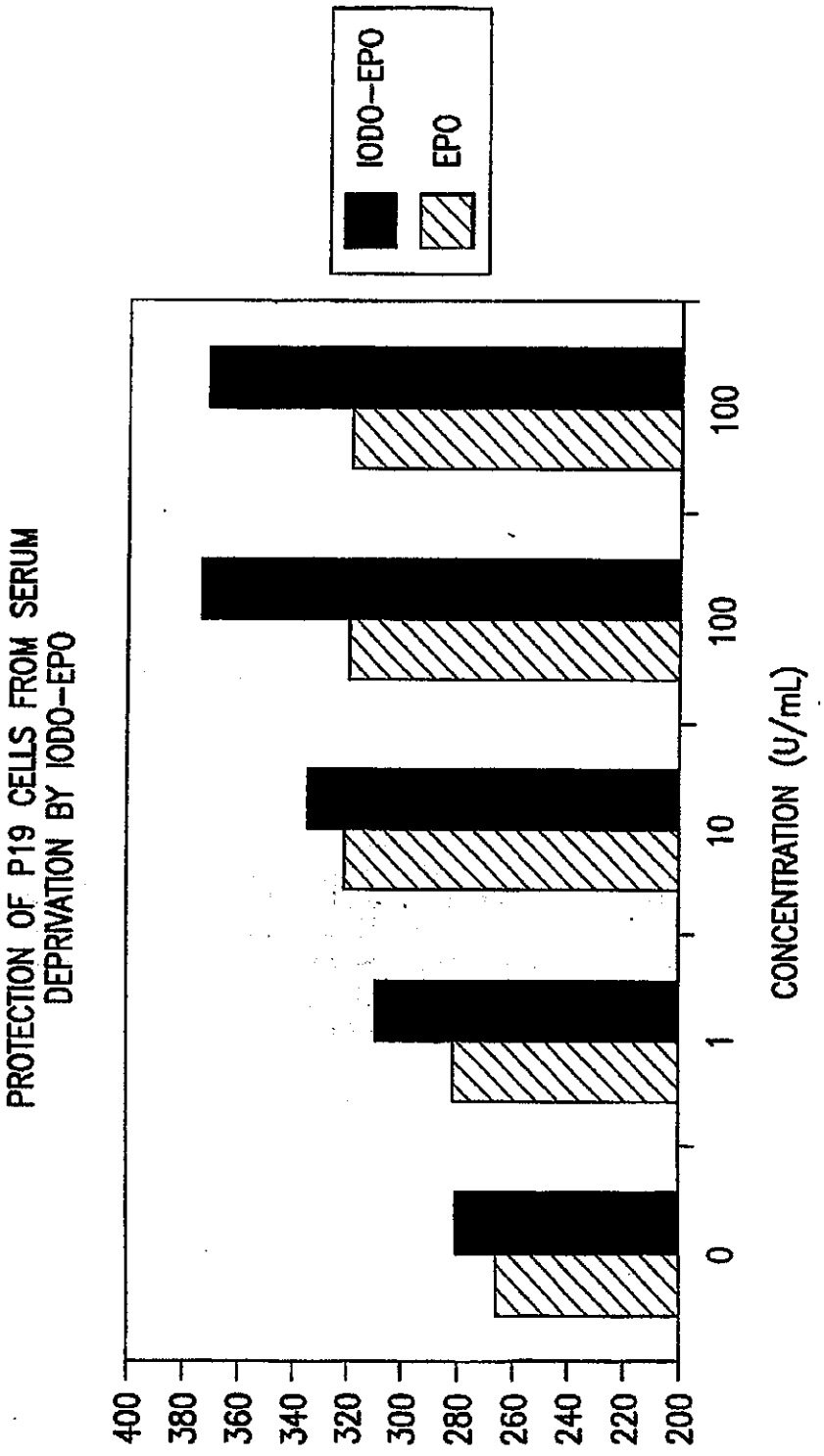

PROTECTION OF P19 CELLS FROM SERUM DEPRIVATION BY IODO-EPO
IODO-EPO
EPO
400
380
360
340
320
300
280
260
240
220
200
0
1
10
100
100
CONCENTRATION (U/mL)

FIG.9

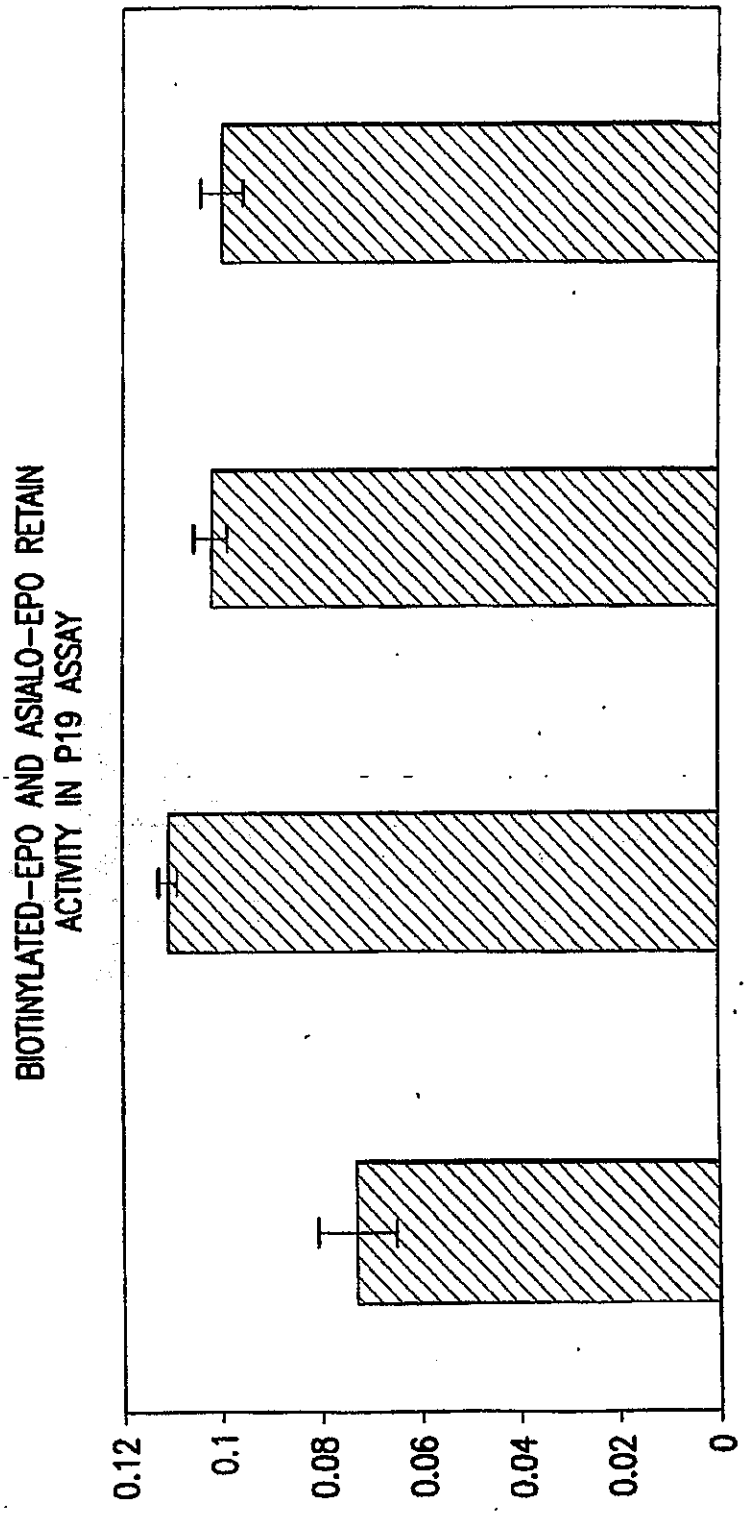

BIOTINYLATED-EPO AND ASIALO-EPO RETAIN ACTIVITY IN P19 ASSAY
0.12
0.1
0.08
0.06
0.04
0.02
0

FIG. 10

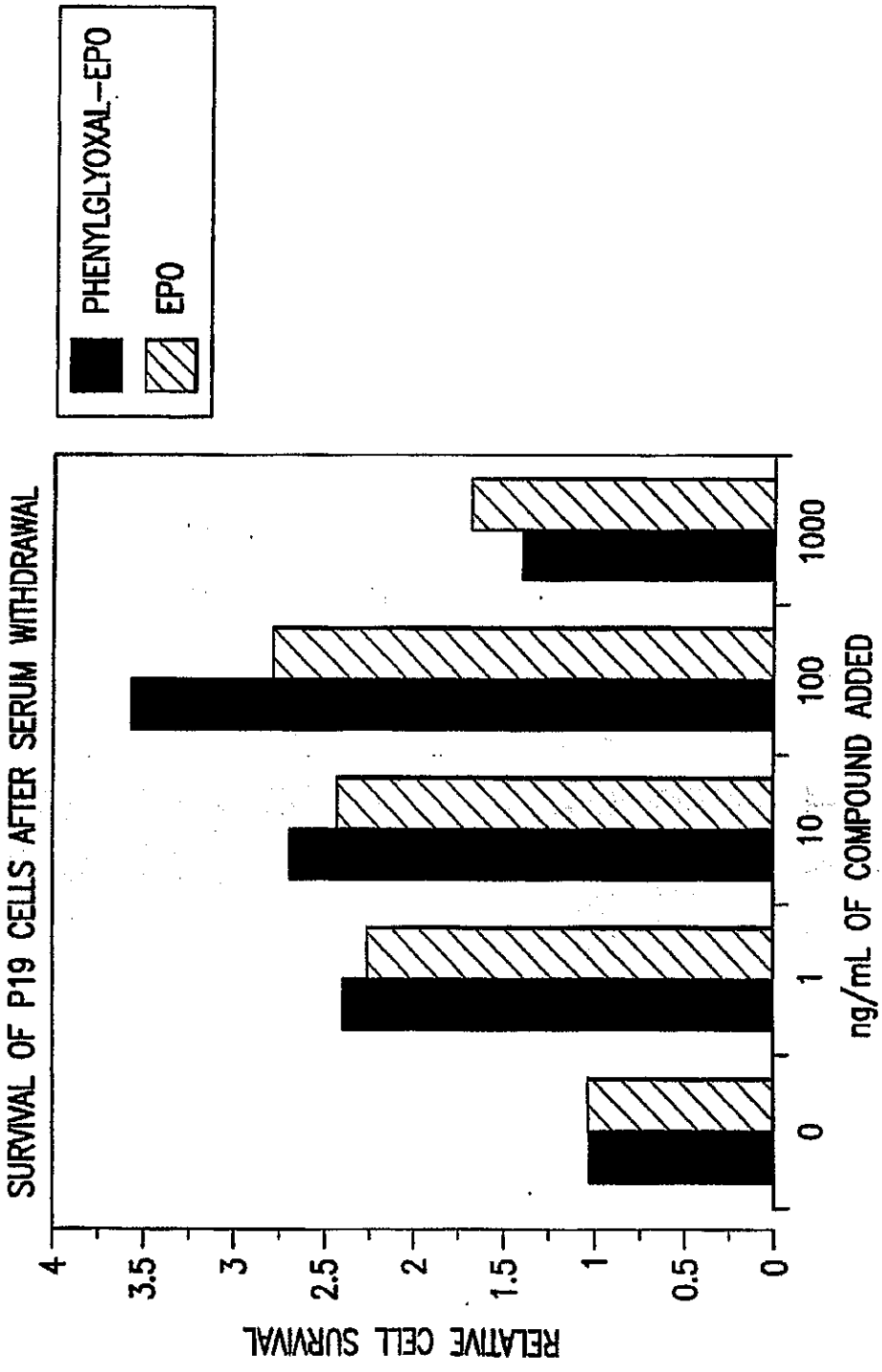

PHENYLGLYOXAL-EPO
EPO
SURVIVAL OF P19 CELLS AFTER SERUM WITHDRAWAL
RELATIVE CELL SURVIVAL
0
0.5
1
1.5
2
2.5
3
3.5
4
0
1
10
100
1000
ng/mL OF COMPOUND ADDED

FIG.11

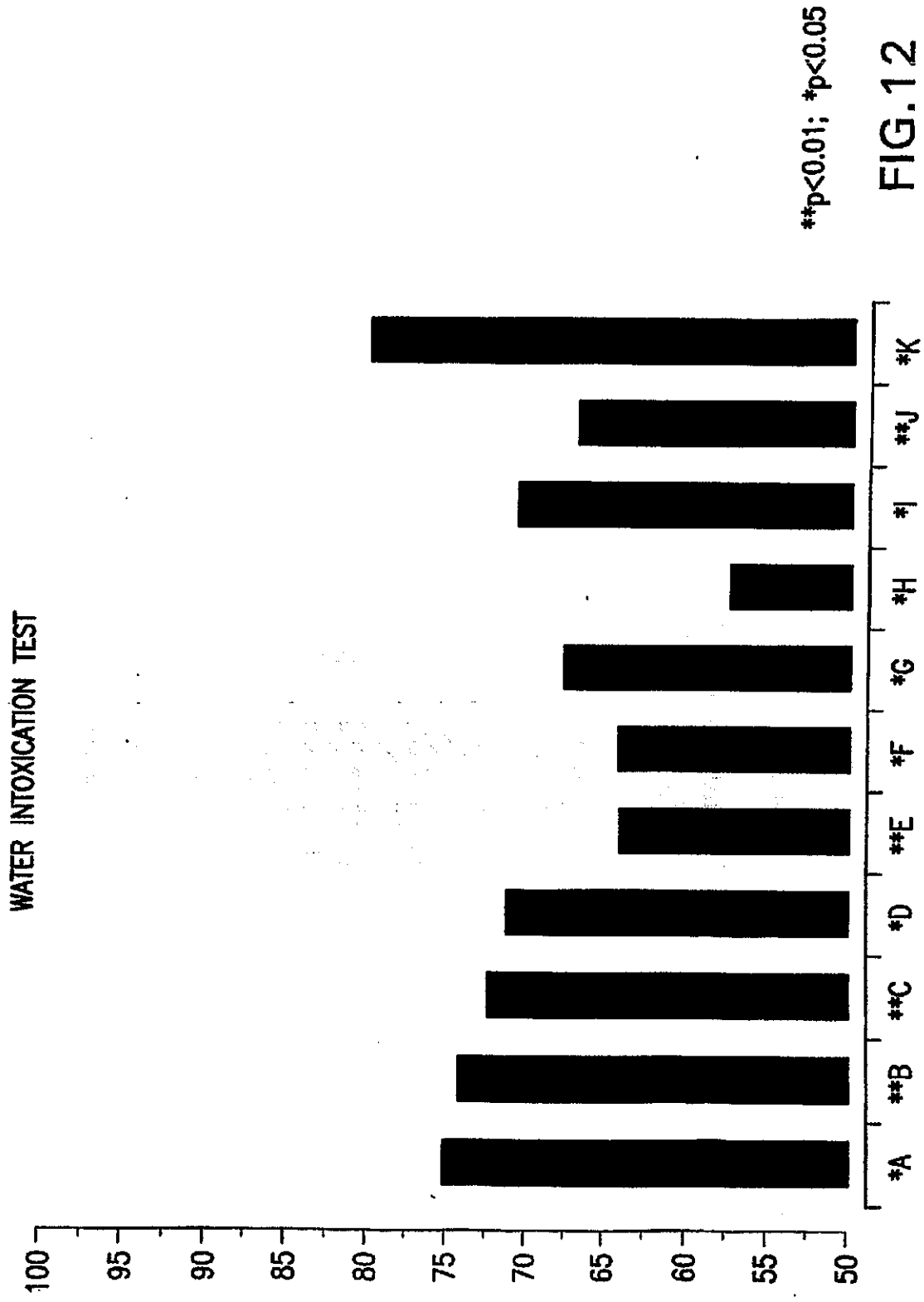

WATER INTOXICATION TEST
100
95
90
85
80
75
70
65
60
55
50
*A
**B
**C
*D
**E
*F
*G
*H
*I
**J
*K
**p<0.01; *p<0.05

FIG. 12

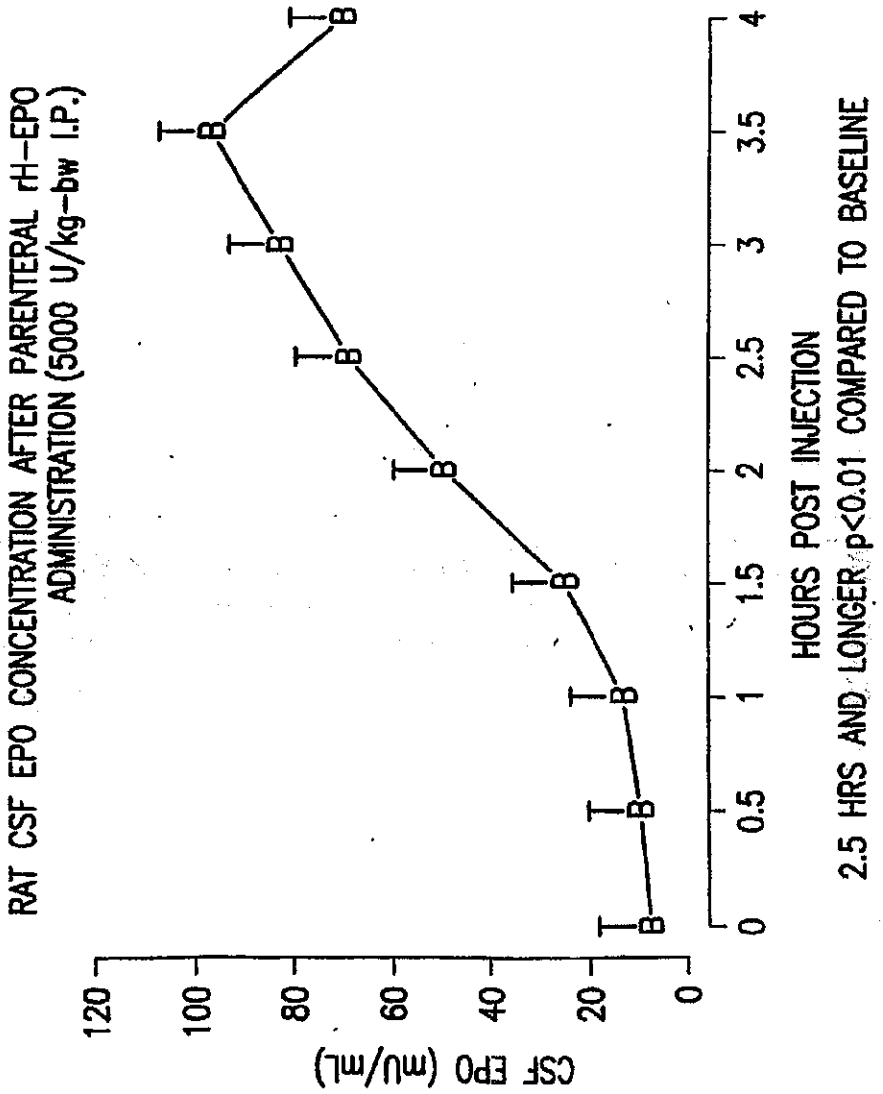

RAT CSF EPO CONCENTRATION AFTER PARENTERAL rH-EPO ADMINISTRATION (5000 U/kg-bw I.P.)
CSF EPO (mU/mL)
120
100
80
60
40
20
0
0
0.5
1
1.5
2
2.5
3
3.5
4
HOURS POST INJECTION
2.5 HRS AND LONGER p<0.01 COMPARED TO BASELINE

FIG.13

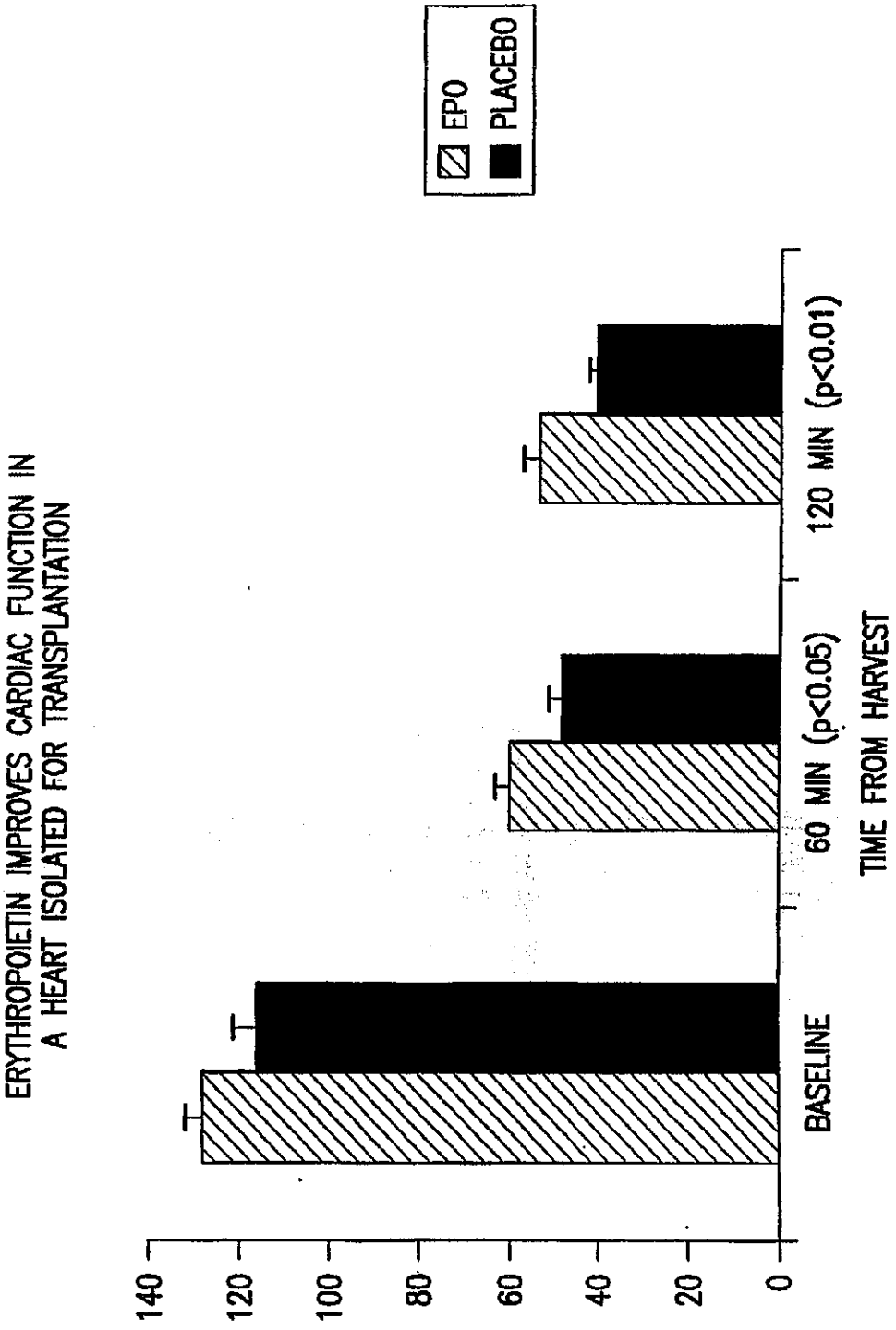
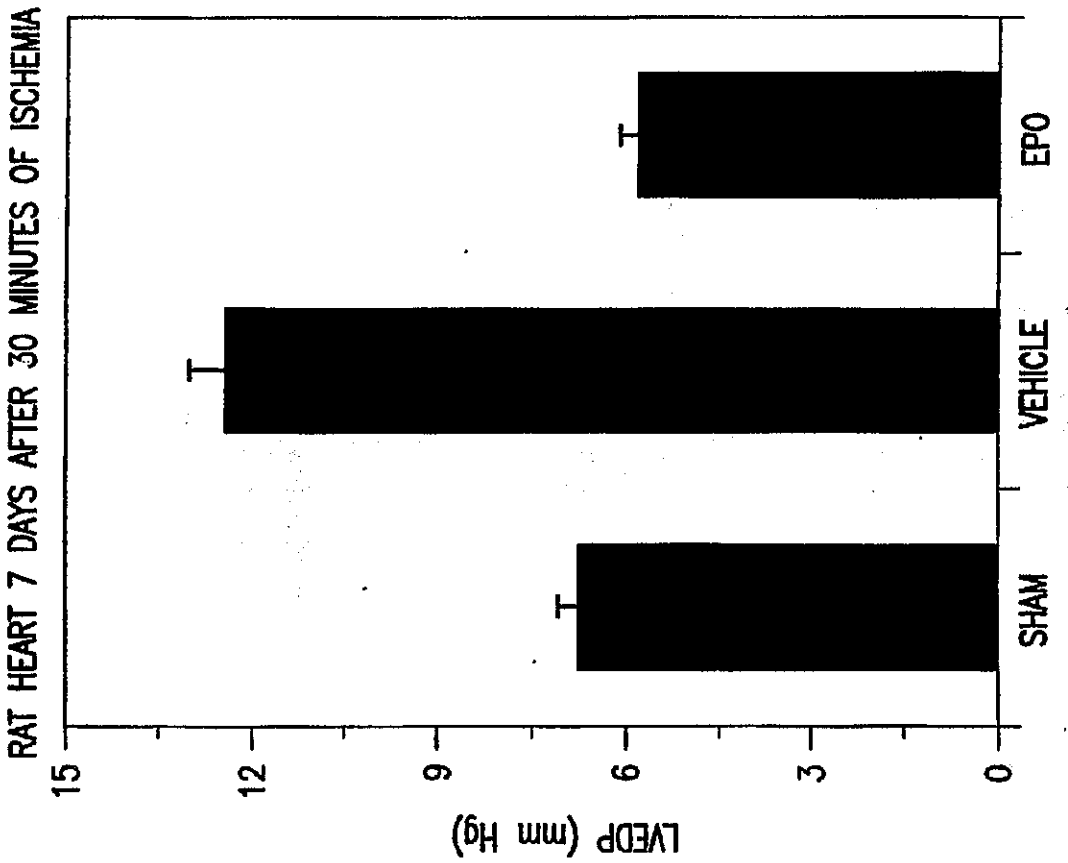

ERYTHROPOIETIN IMPROVES CARDIAC FUNCTION IN A HEART ISOLATED FOR TRANSPLANTATION
EPO
PLACEBO
140
120
100
80
60
40
20
0
BASELINE
60 MIN (p<0.05)
120 MIN (p<0.01)
TIME FROM HARVEST

FIG. 14

FIG. 15


RAT HEART 7 DAYS AFTER 30 MINUTES OF ISCHEMIA
LVEDP (mm Hg)
15
12
9
6
3
0
SHAM
VEHICLE
EPO

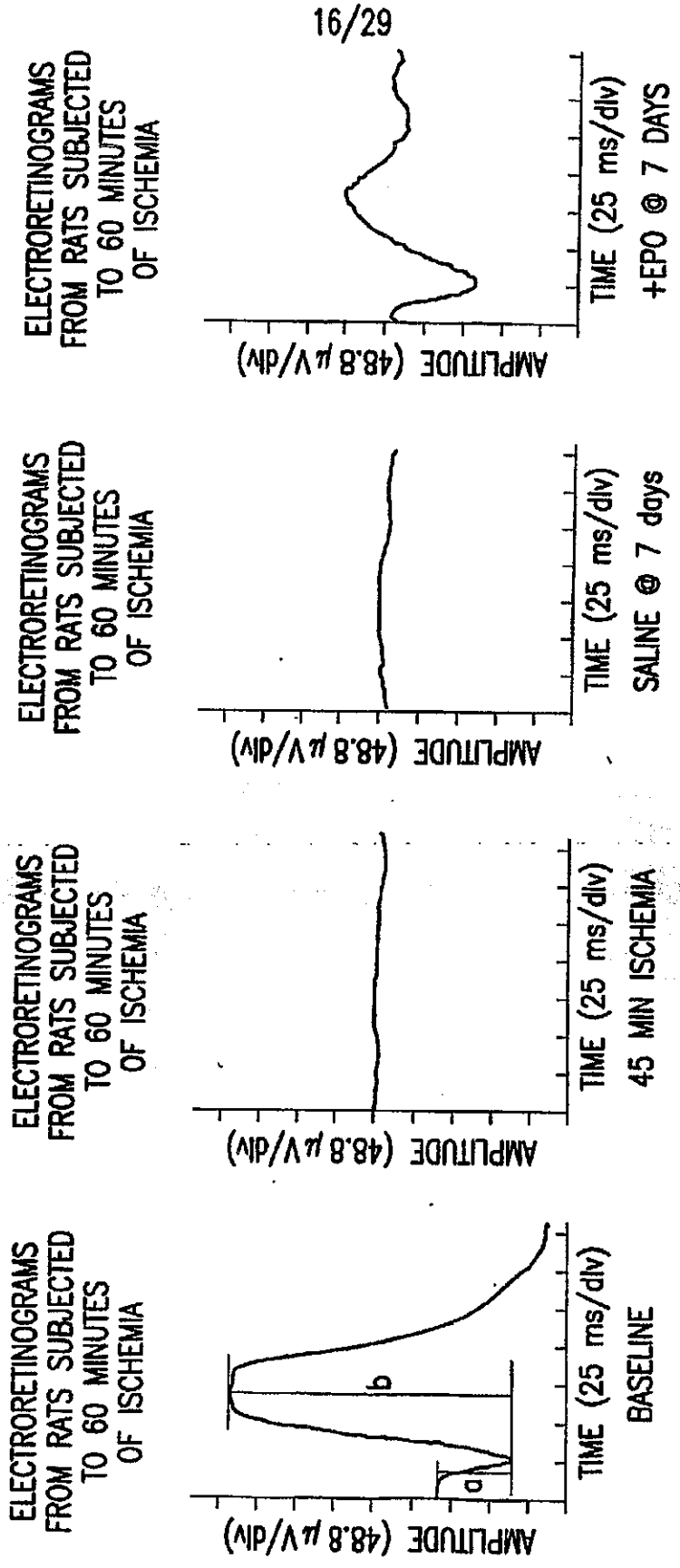



FIG.16A FIG.16B FIG.16C FIG.16D

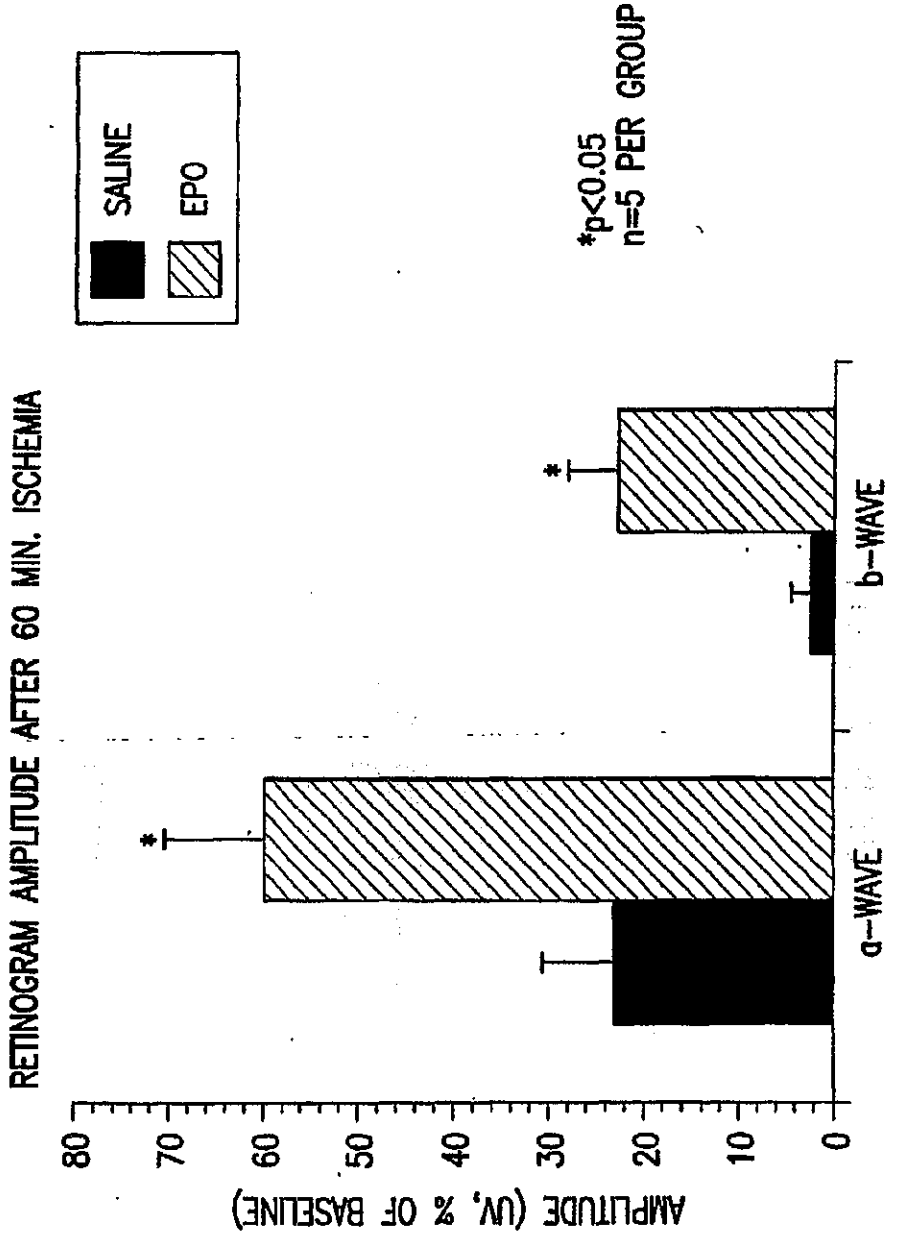

RETINOGRAM AMPLITUDE AFTER 60 MIN. ISCHEMIA
SALINE
EPO
*p<0.05
n=5 PER GROUP
AMPLITUDE (UV, % OF BASELINE)
80
70
60
50
40
30
20
10
0
a-WAVE
b-WAVE
*
*

FIG.17

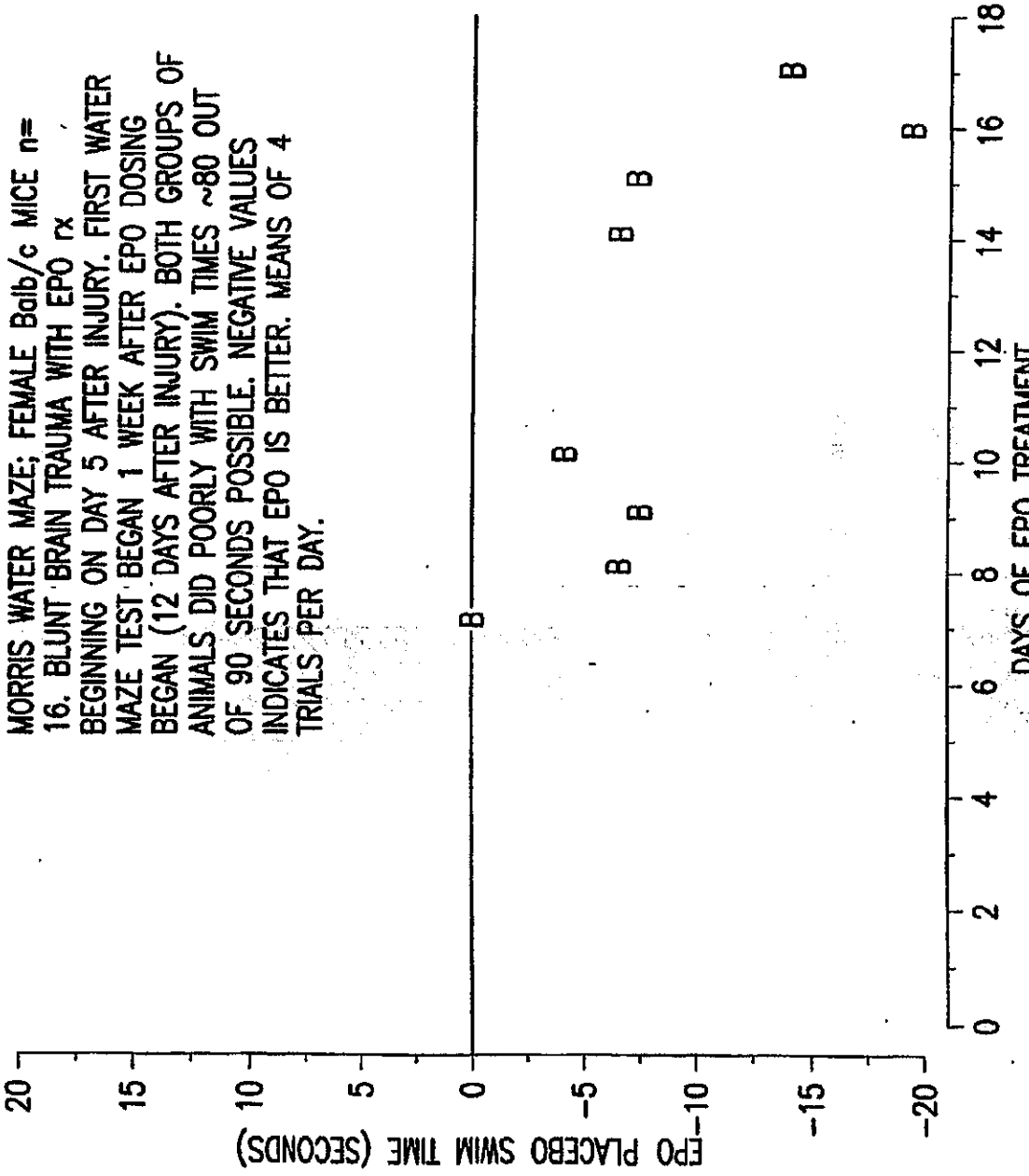

MORRIS WATER MAZE; FEMALE Balb/c MICE n=
16. BLUNT BRAIN TRAUMA WITH EPO rx
BEGINNING ON DAY 5 AFTER INJURY. FIRST WATER
MAZE TEST BEGAN 1 WEEK AFTER EPO DOSING
BEGAN (12 DAYS AFTER INJURY). BOTH GROUPS OF
ANIMALS DID POORLY WITH SWIM TIMES ~80 OUT
OF 90 SECONDS POSSIBLE. NEGATIVE VALUES
INDICATES THAT EPO IS BETTER. MEANS OF 4
TRIALS PER DAY.
EPO PLACEBO SWIM TIME (SECONDS)
20
15
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
16
18
DAYS OF EPO TREATMENT
B
B
B
B
B
B
B
B

FIG.18

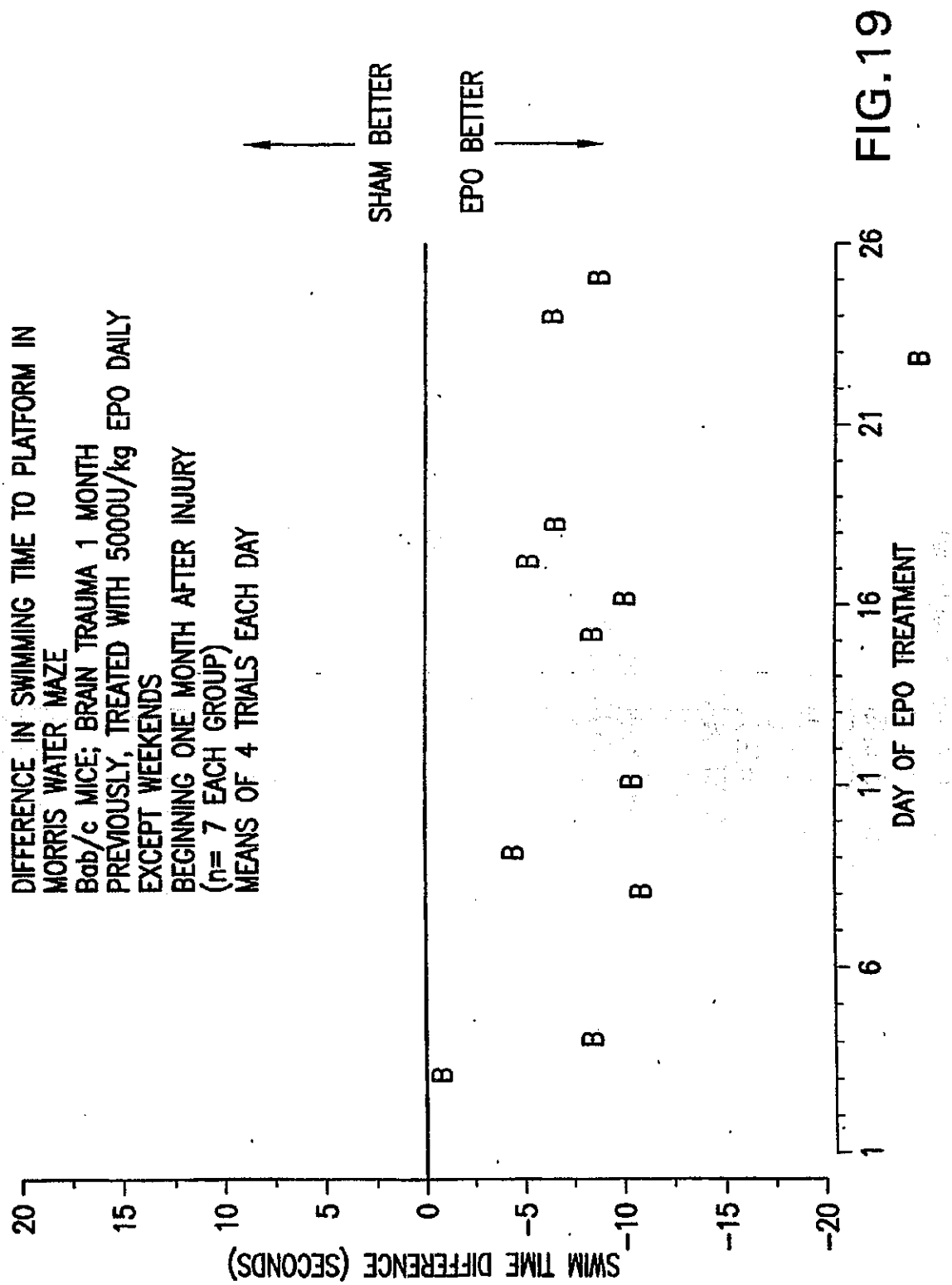

DIFFERENCE IN SWIMMING TIME TO PLATFORM IN MORRIS WATER MAZE
Bab/c MICE; BRAIN TRAUMA 1 MONTH PREVIOUSLY, TREATED WITH 5000U/kg EPO DAILY EXCEPT WEEKENDS
BEGINNING ONE MONTH AFTER INJURY
(n= 7 EACH GROUP)
MEANS OF 4 TRIALS EACH DAY
SHAM BETTER
EPO BETTER
SWIM TIME DIFFERENCE (SECONDS)
DAY OF EPO TREATMENT

FIG.19

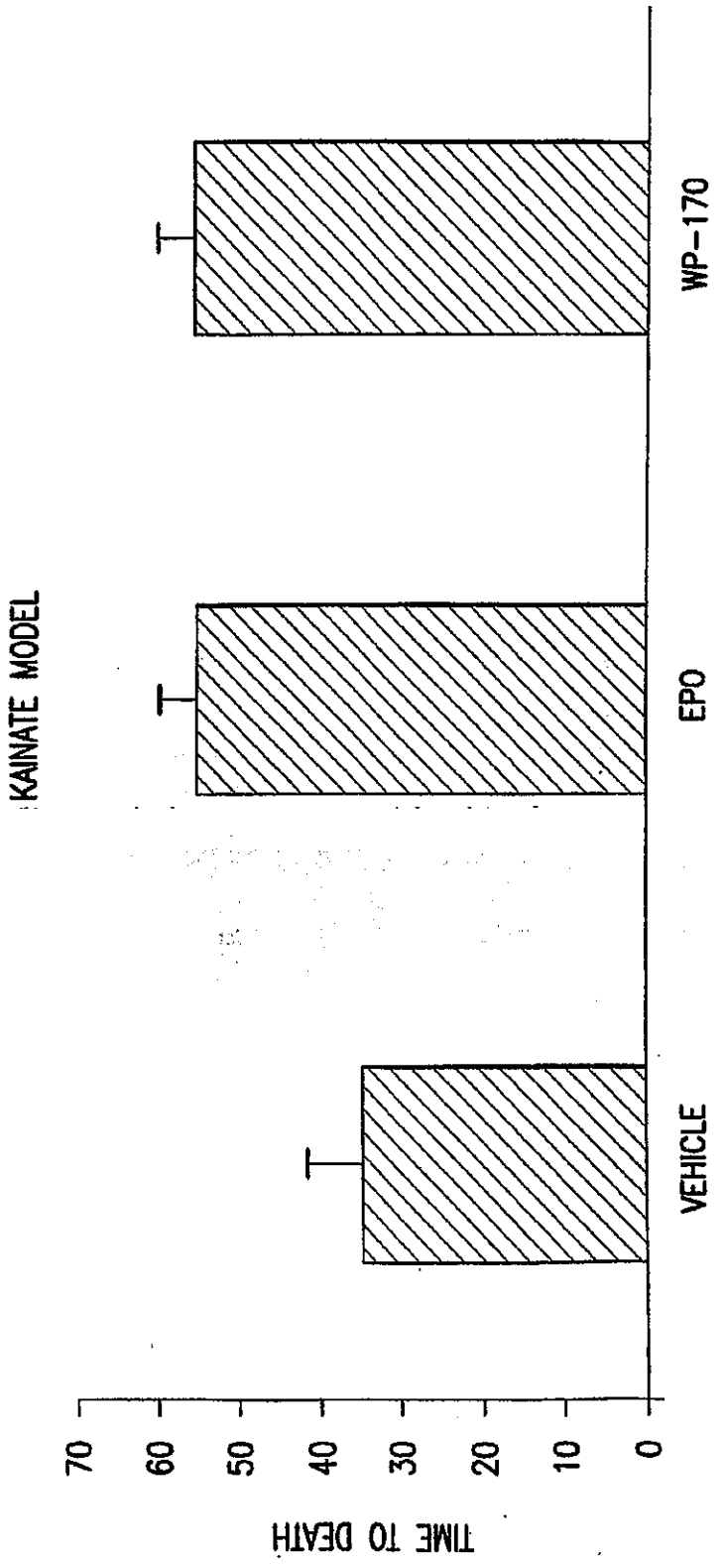
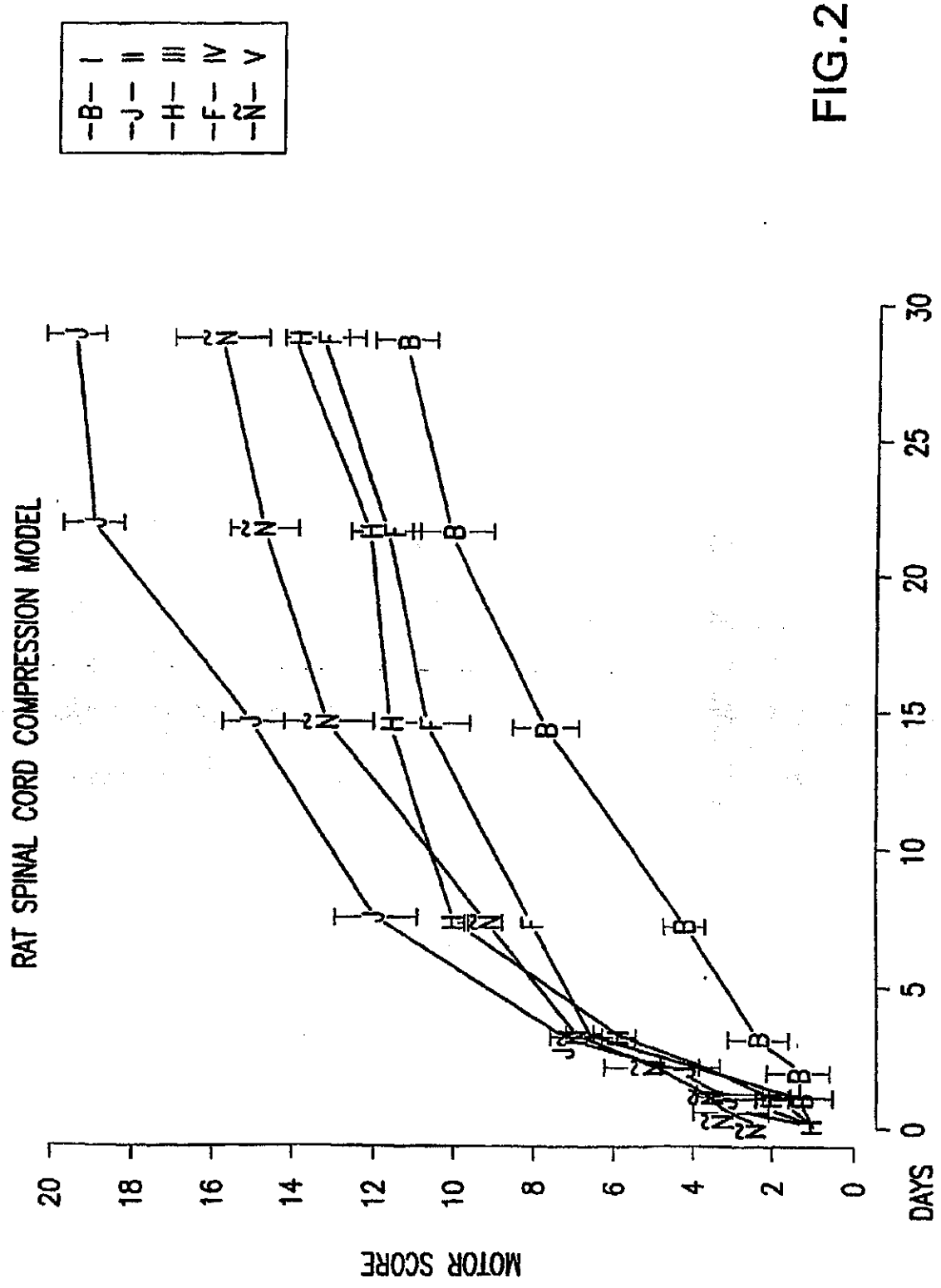

KAINATE MODEL
VEHICLE
EPO
WP-170
TIME TO DEATH
0
10
20
30
40
50
60
70

FIG.20

FIG.21


I
II
III
IV
V
B
J
H
F
N
RAT SPINAL CORD COMPRESSION MODEL
MOTOR SCORE
DAYS
0
2
4
6
8
10
12
14
16
18
20
0
5
10
15
20
25
30

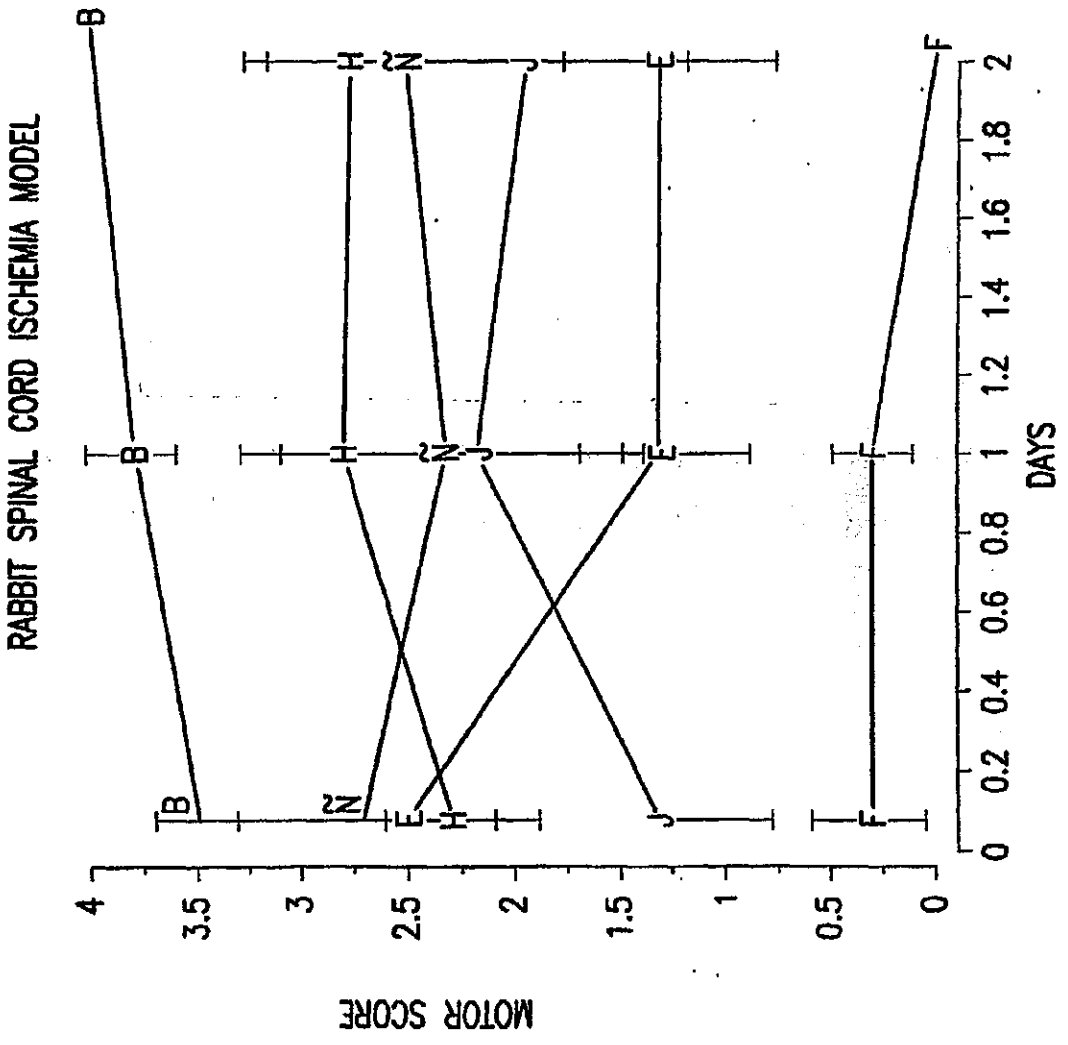

RABBIT SPINAL CORD ISCHEMIA MODEL
MOTOR SCORE
DAYS
B
J
H
N2
E
F
V
IV
VI
I
II
III
4
3.5
3
2.5
2
1.5
1
0.5
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2

FIG.22

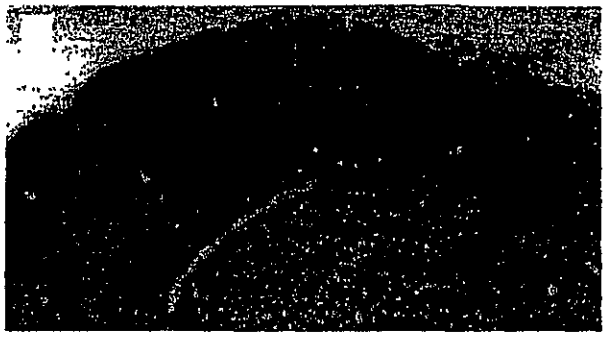


FIG.23A

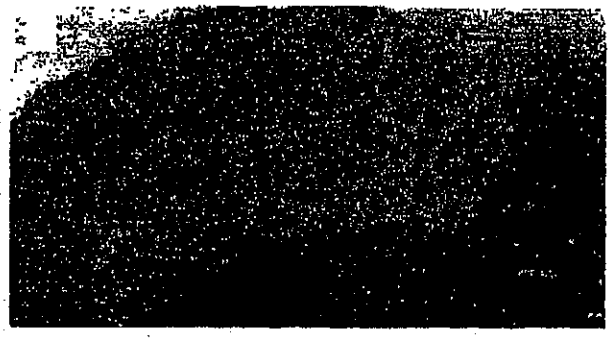


FIG.23B



FIG.23C

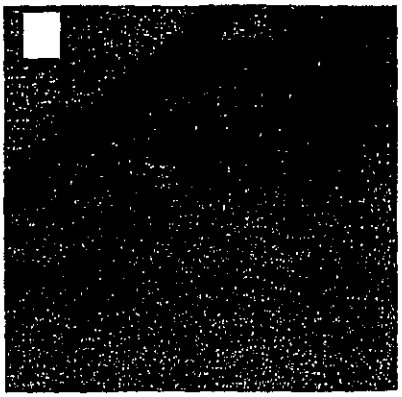


FIG.24A

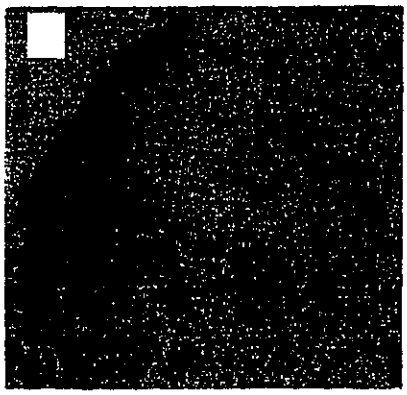


FIG.24B

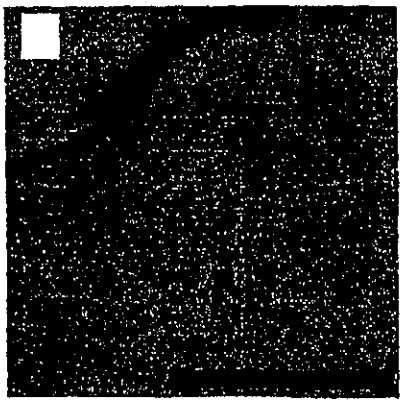


FIG 24C

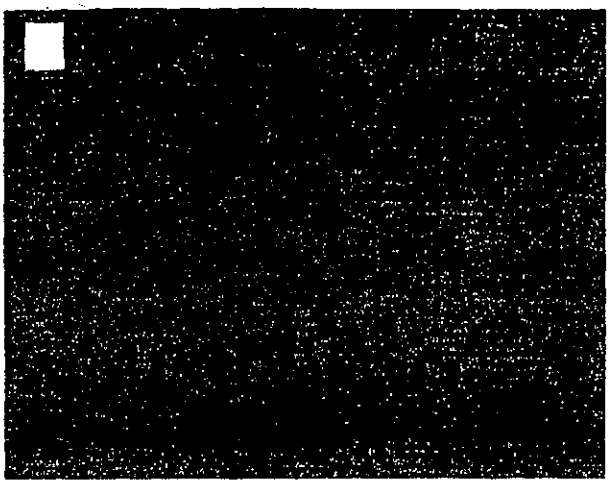


FIG.25A

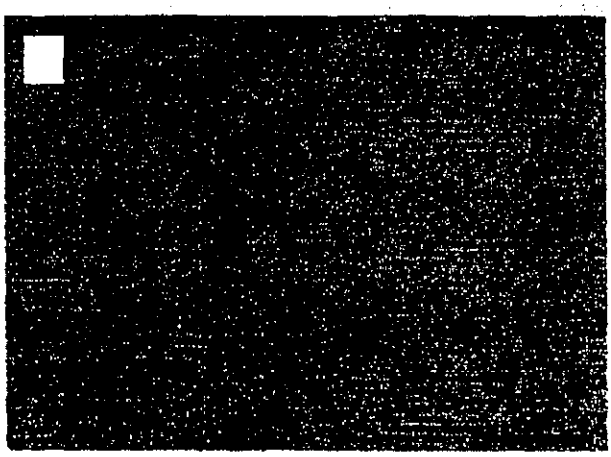


FIG.25B

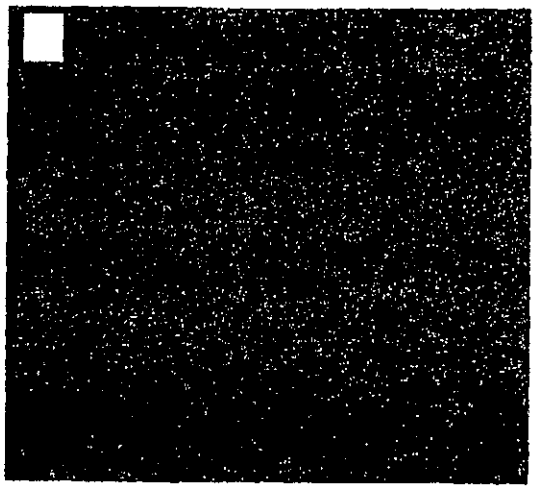


FIG.26A

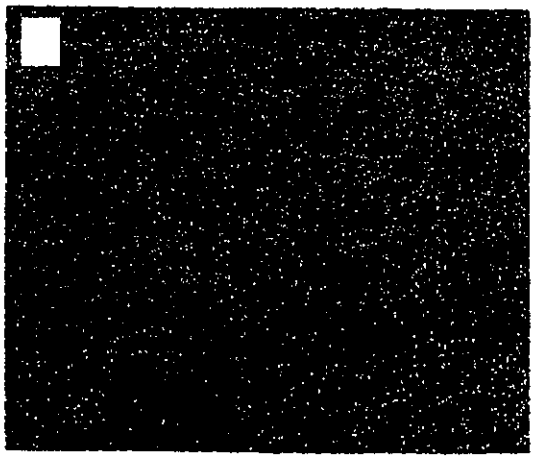


FIG.26B

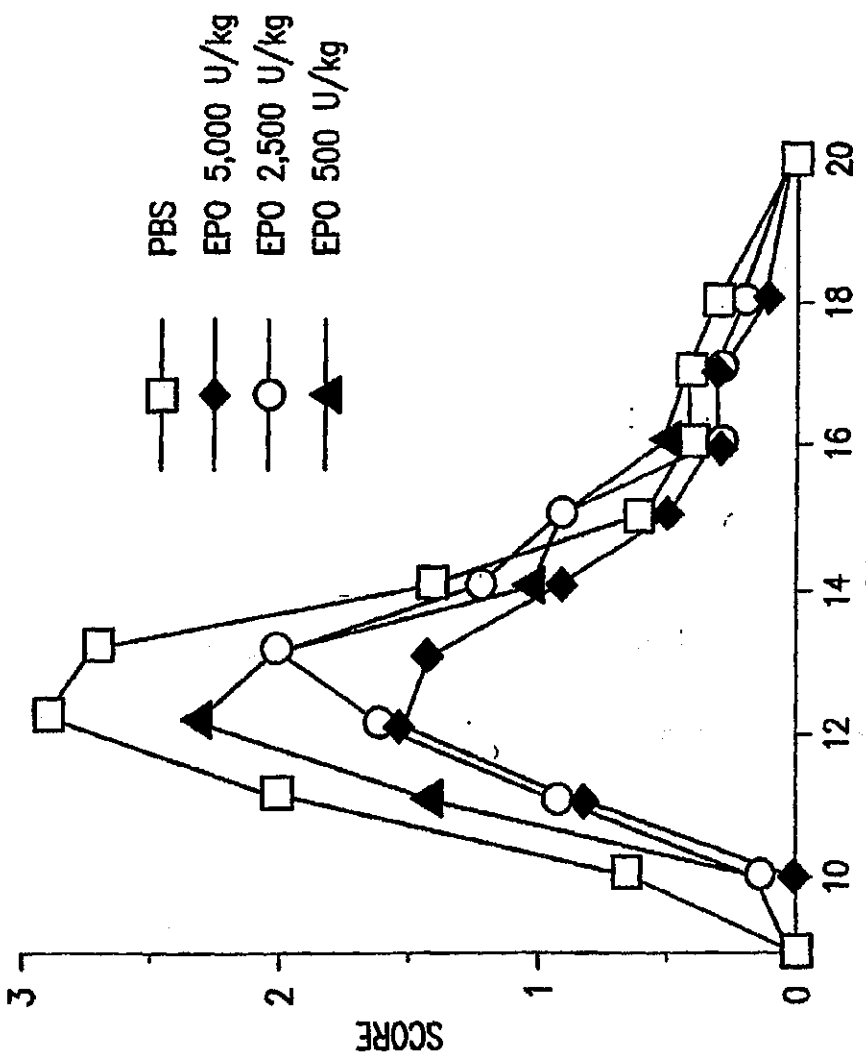

PBS
EPO 5,000 U/kg
EPO 2,500 U/kg
EPO 500 U/kg
SCORE
0
1
2
3
DAYS
10
12
14
16
18
20

FIG.27

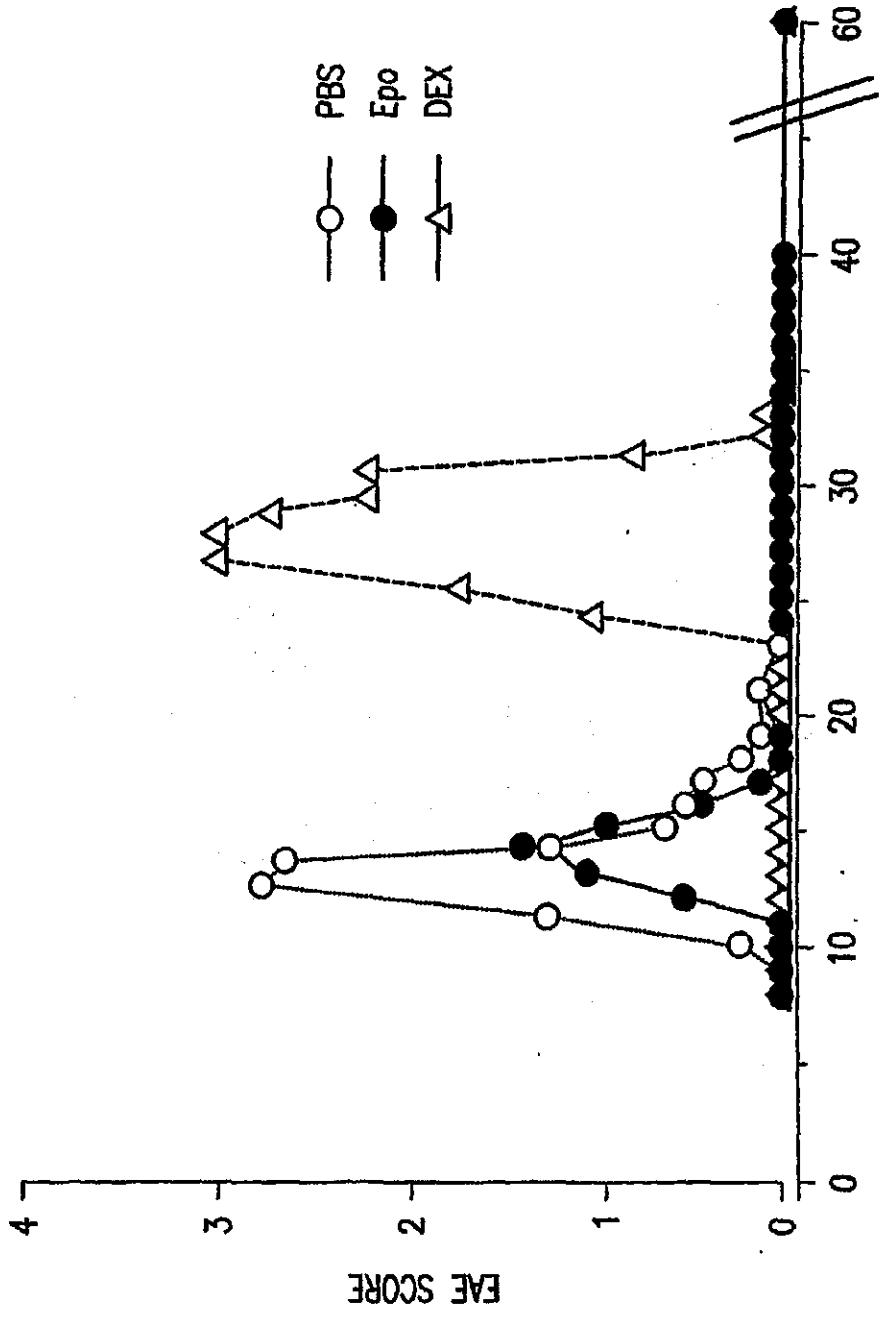

PBS
Epo
DEX
EAE SCORE
0
1
2
3
4
DAYS FROM IMMUNIZATION
0
10
20
30
40
60

FIG.28

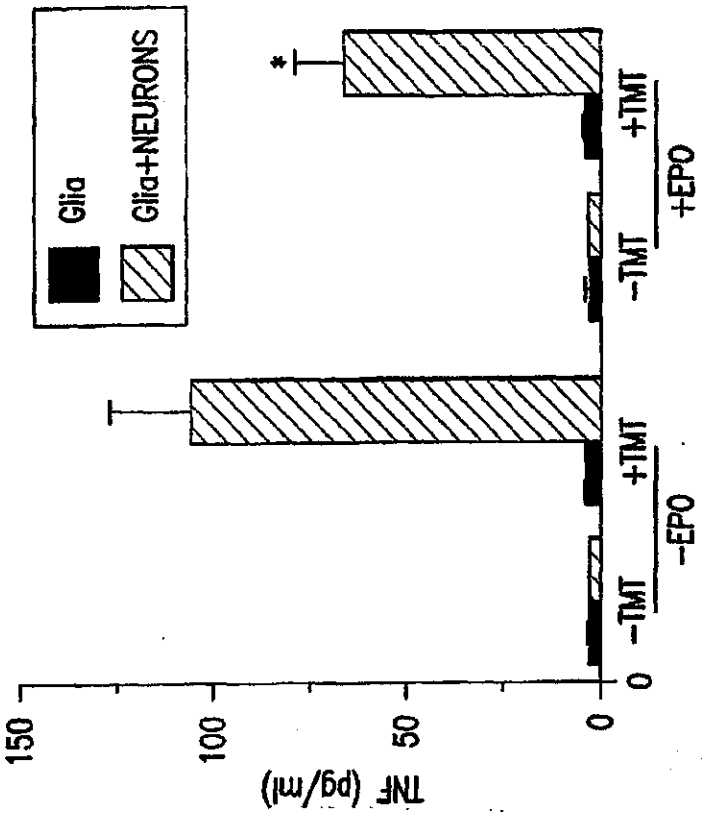



FIG.29B

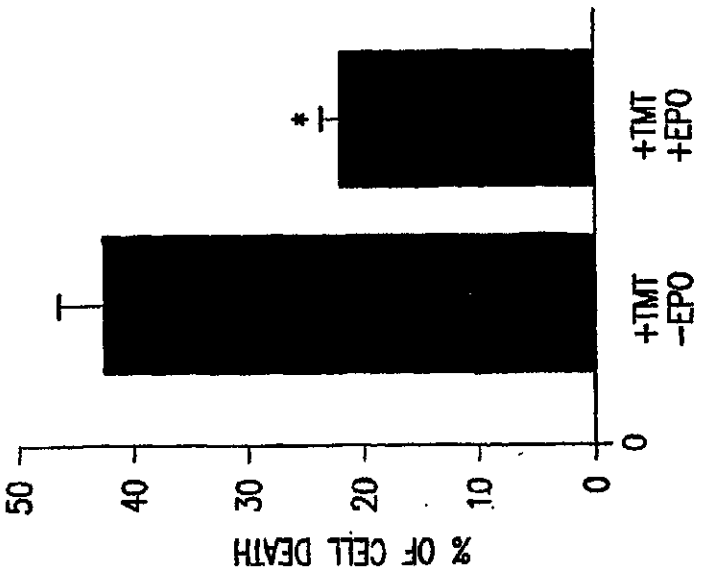



FIG.29A

SEQUENCE LISTING

<110> The Kenneth S. Warren Institute, Inc.

<120> TISSUE PROTECTIVE CYTOKINES FOR THE PROTECTION, RESTORATION, AND ENHANCEMENT OF RESPONSIVE CELLS, TISSUES AND ORGANS

<130> 10165-026-228

<140>
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<150> 10/188,905
<151> 2002-07-03

<160> 4

<170> PatentIn version 3.0

<210> 1
<211> 5
<212> PRT
<213> Artificial

<220>
<223> Description of Artificial Sequence: Functional Domains

<400> 1
Val Leu Gln Arg Tyr
1 5

<210> 2
<211> 8
<212> PRT
<213> Artificial

<220>
<223> Description of Artificial Sequence: Functional Domains

<400> 2
Thr Lys Val Asn Phe Tyr Ala Trp
1 5

<210> 3
<211> 9
<212> PRT
<213> Artificial

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<223> Description of Artificial Sequence: Functional Domains

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Ser Gly Leu Arg Ser Leu Thr Thr Leu
1 5

<210> 4
<211> 6
<212> PRT
<213> Artificial

<220>

<223> Description of Artificial Sequence: Functional Domains

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Ser Asn Phe Leu Arg Gly
1 5