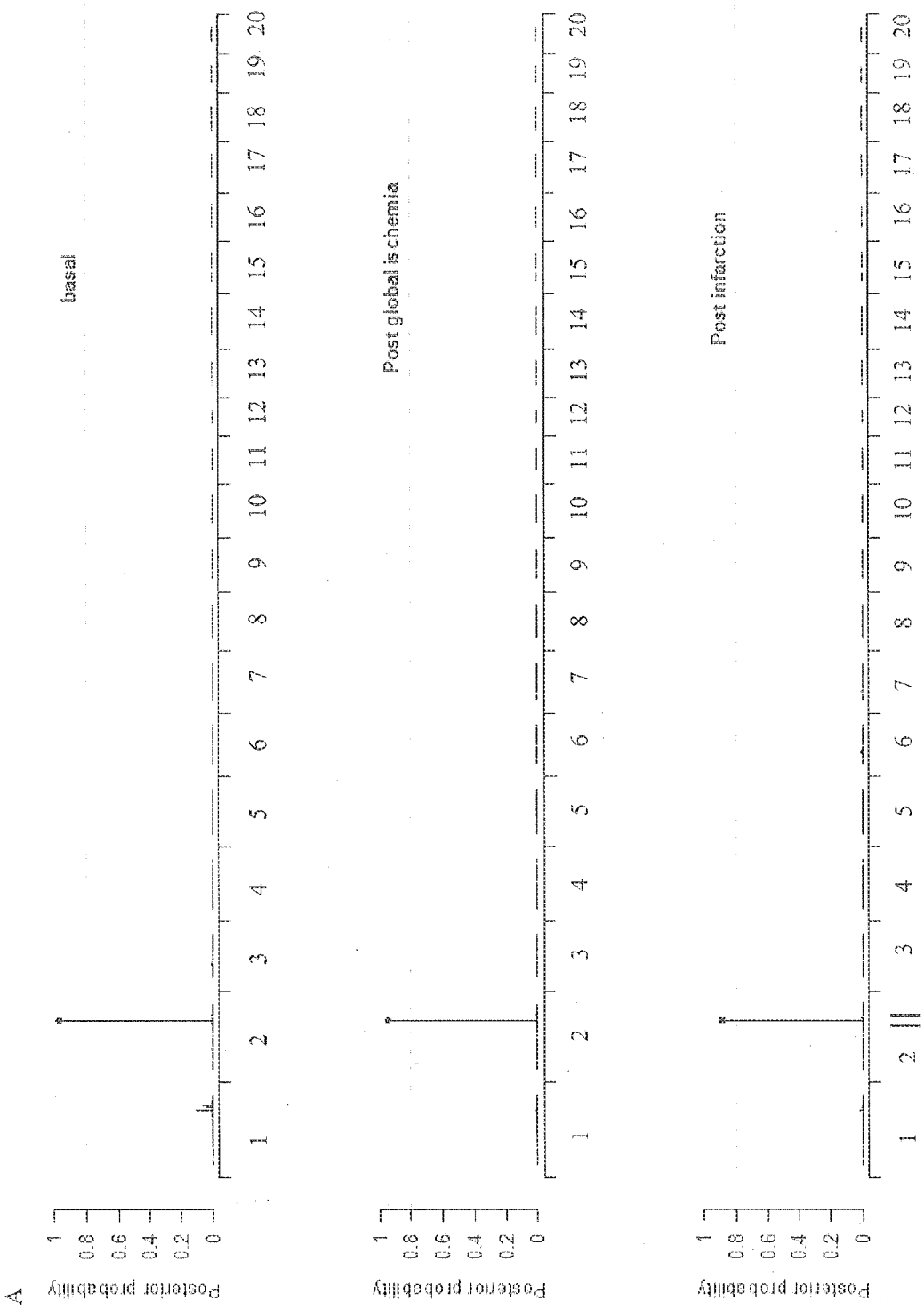
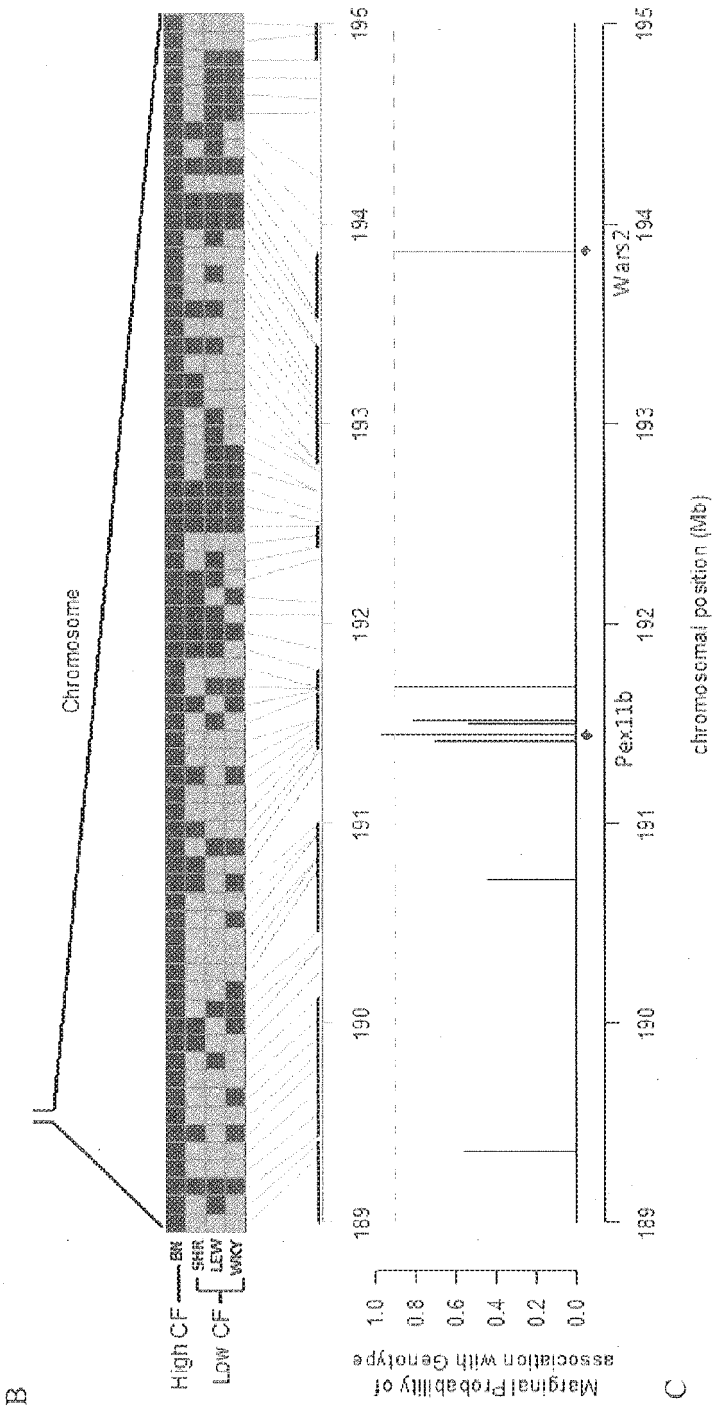
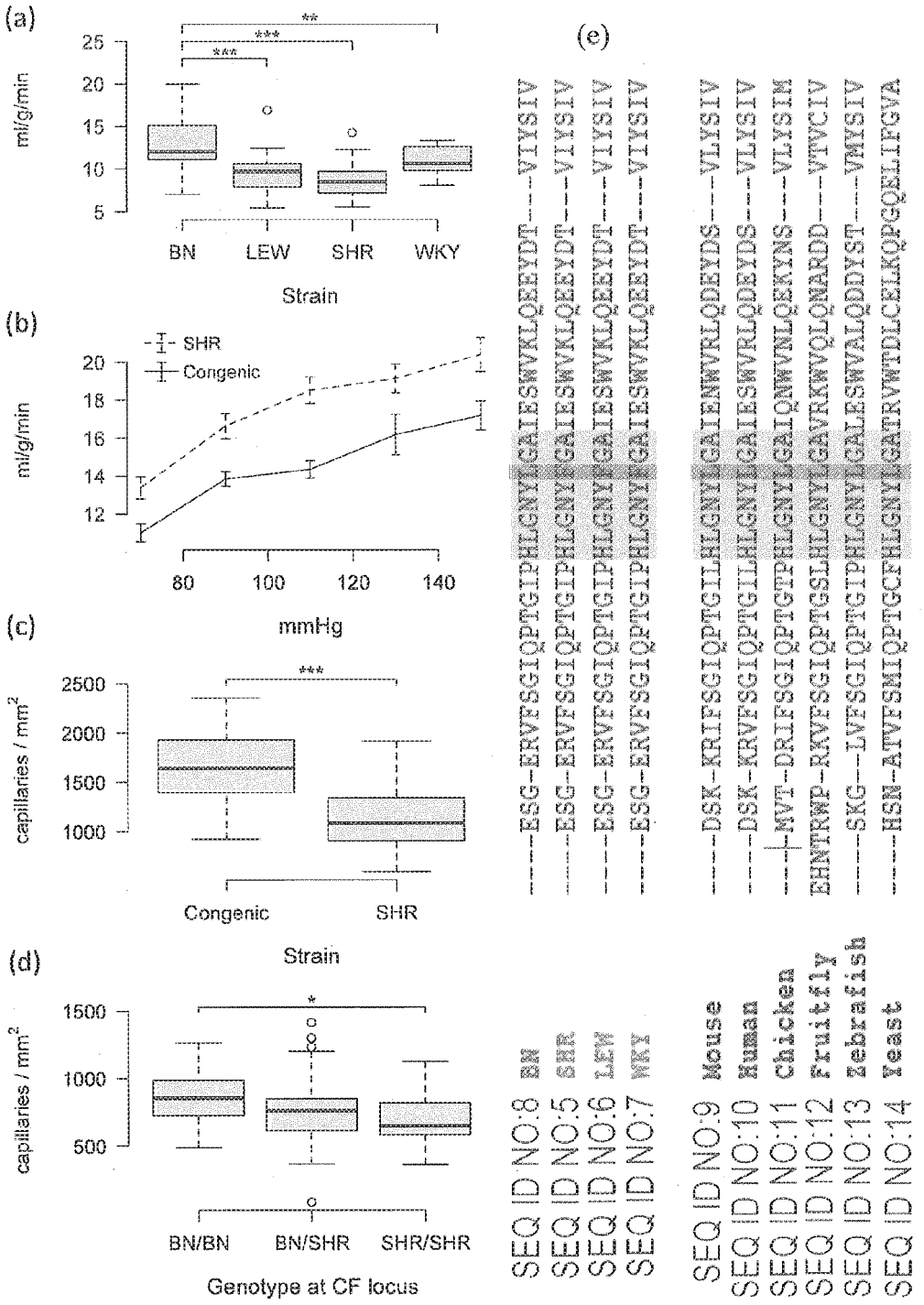

A
basal
Post global ischemia
Post infarction
Posterior probability
1
0.8
0.6
0.4
0.2
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

FIG. 1A



FIGS. 1B AND 1C


(a)
ml/g/min
BN
LEW
SHR
WKY
Strain
(b)
SHR
Congenic
ml/g/min
mmHg
(c)
capillaries / mm2
Congenic
SHR
Strain
(d)
capillaries / mm2
BN/BN
BN/SHR
SHR/SHR
Genotype at CF locus
(e)
SEQ ID NO:8 BN
SEQ ID NO:5 SHR
SEQ ID NO:6 LEW
SEQ ID NO:7 WKY
SEQ ID NO:9 Mouse
SEQ ID NO:10 Human
SEQ ID NO:11 Chicken
SEQ ID NO:12 Fruitfly
SEQ ID NO:13 Zebrafish
SEQ ID NO:14 Yeast

FIGS. 2A-2E

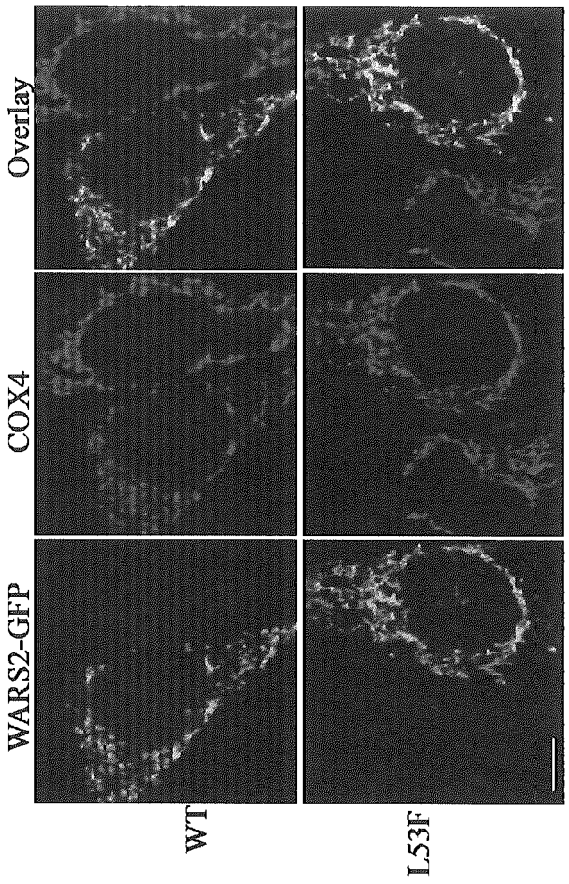


FIG. 3

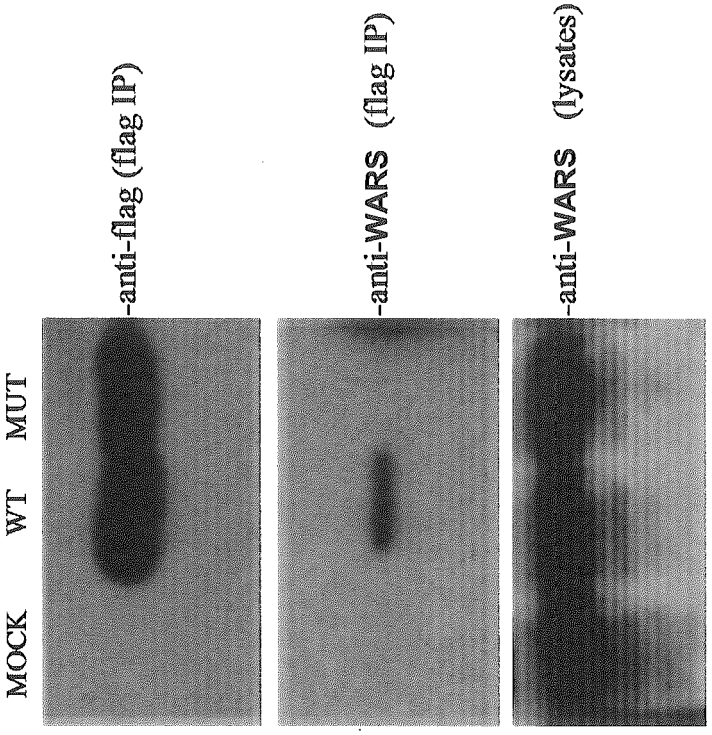

MOCK
WT
MUT
-anti-flag (flag IP)
-anti-WARS (flag IP)
-anti-WARS (lysates)

FIG. 4

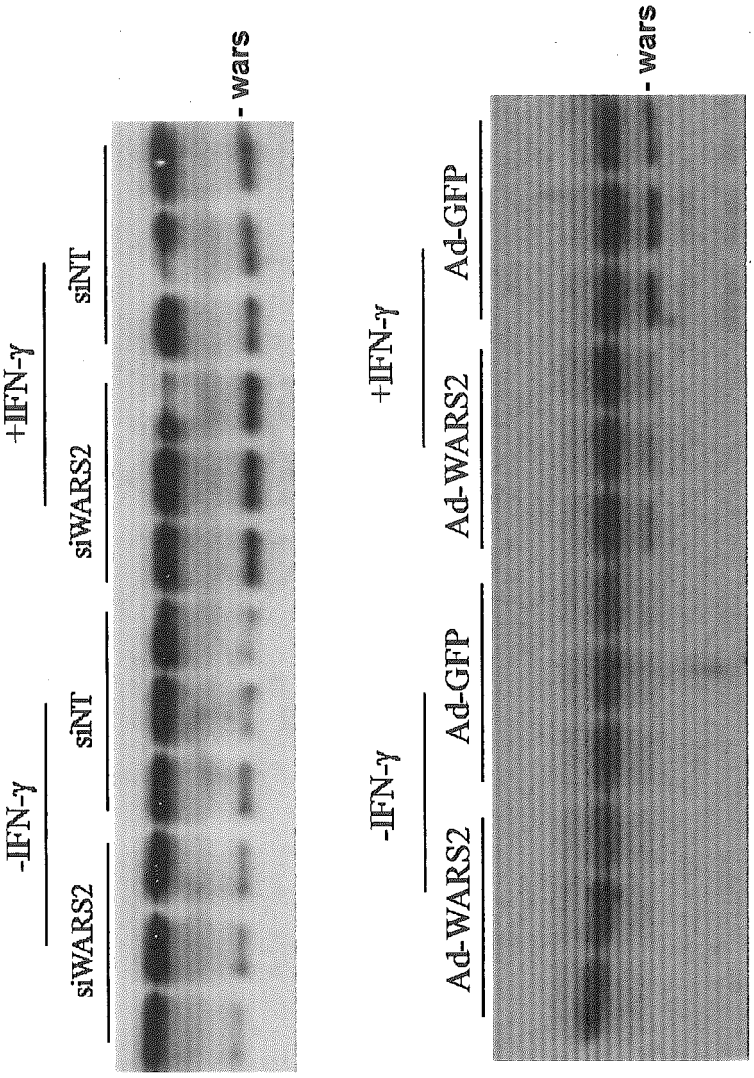

-IFN-γ
+IFN-γ
siWARS2
siNT
siWARS2
siNT
- wars
-IFN-γ
+IFN-γ
Ad-WARS2
Ad-GFP
Ad-WARS2
Ad-GFP
- wars

FIG. 5

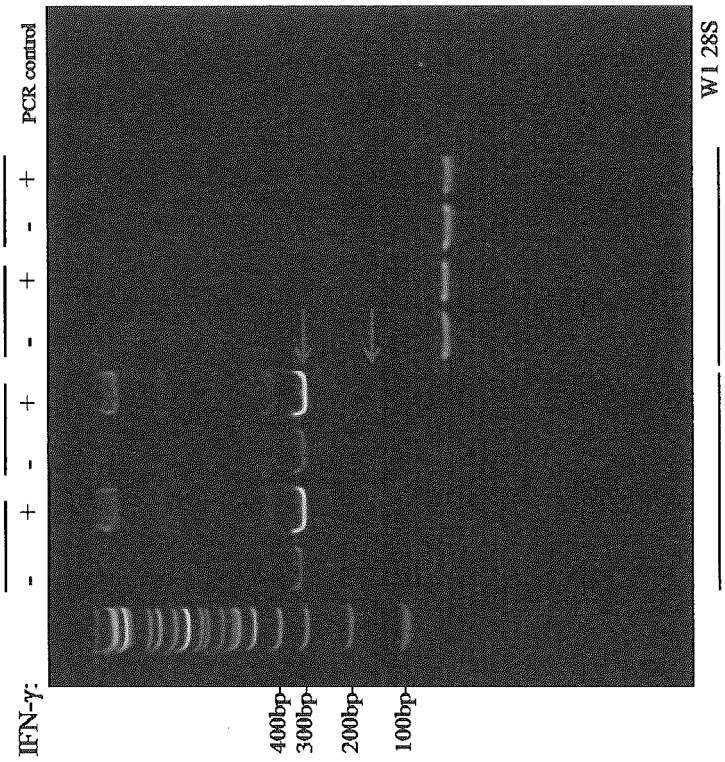

IFN-γ:
siNT
siWARS2
siNT
siWARS2
PCR control
- + - + - + +
400bp
300bp
200bp
100bp
WARS
28S
W1 28S

FIG. 6A

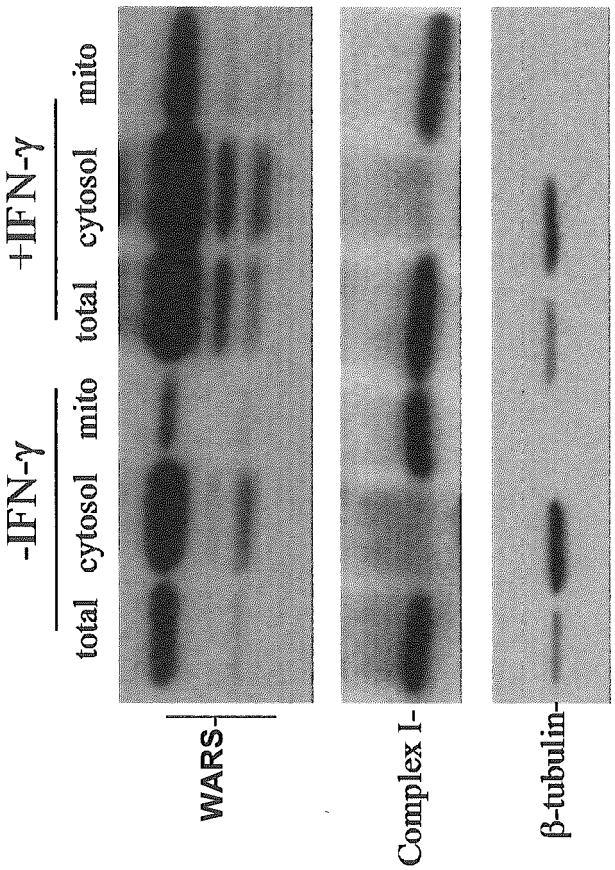

-IFN-γ
+IFN-γ
total
cytosol
mito
total
cytosol
mito
WARS
Complex I
β-tubulin

FIG. 6B

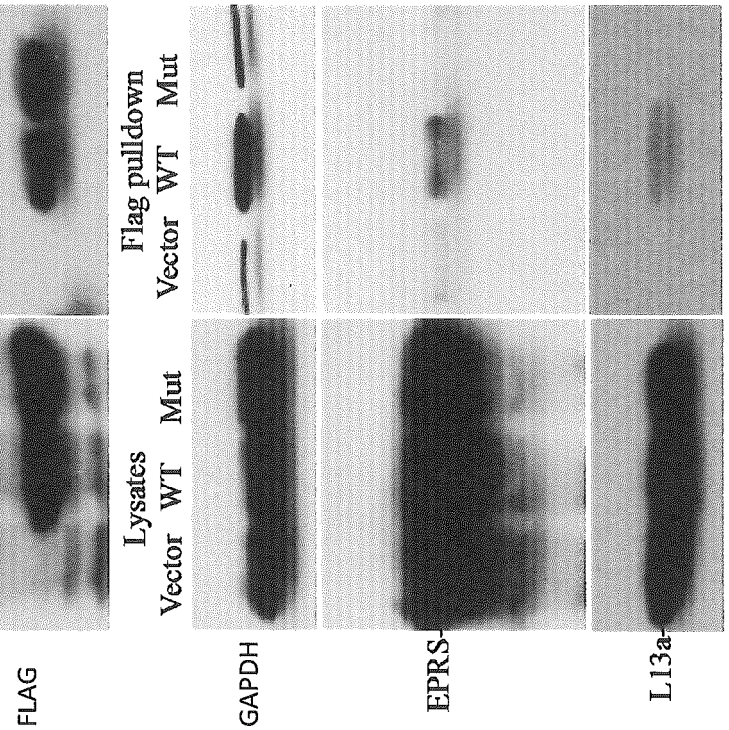
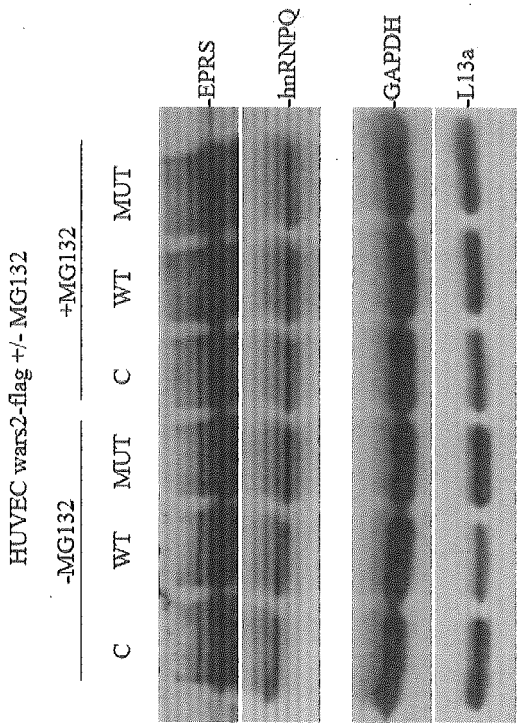

Lysates
Vector WT Mut
purified -Flag
Vector WT Mut
Lysates
Vector WT Mut
Flag pulldown
Vector WT Mut
FLAG
GAPDH
EPRS
L13a

FIG. 7


HUVEC wars2-flag +/- MG132
-MG132
+MG132
C
WT
MUT
C
WT
MUT
-EPRS
-hnRNPQ
-GAPDH
-L13a

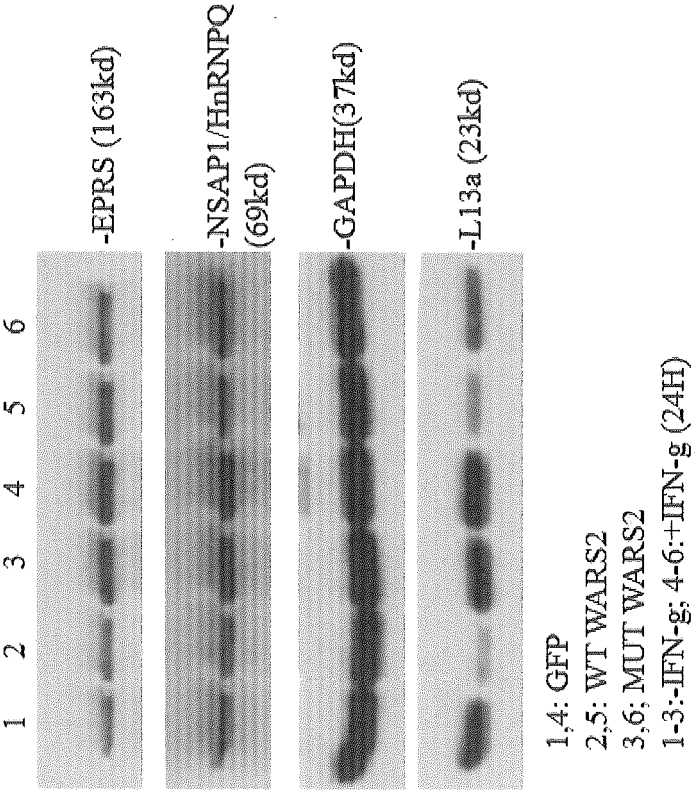

1 2 3 4 5 6
-EPRS (163kd)
-NSAP1/HnRNPQ (69kd)
-GAPDH(37kd)
-L13a (23kd)
1,4: GFP
2,5: WT WARS2
3,6; MUT WARS2
1-3:-IFN-g; 4-6:+IFN-g (24H)

FIG. 8

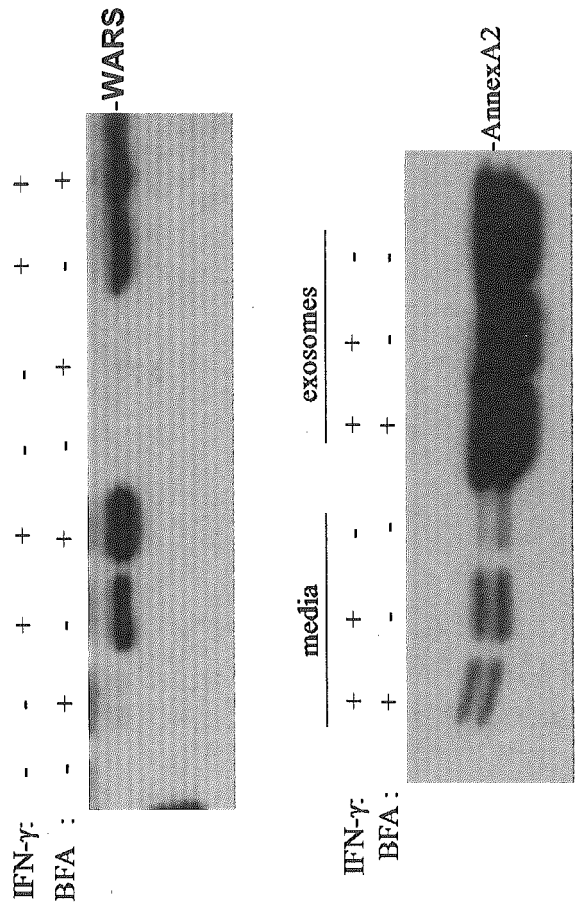

media
exosomes
IFN-γ: - - + + - - + +
BFA : - + - + - + - +
-WARS
media
exosomes
IFN-γ: + + - + + -
BFA : + - - + - -
-AnnexA2

FIG. 9

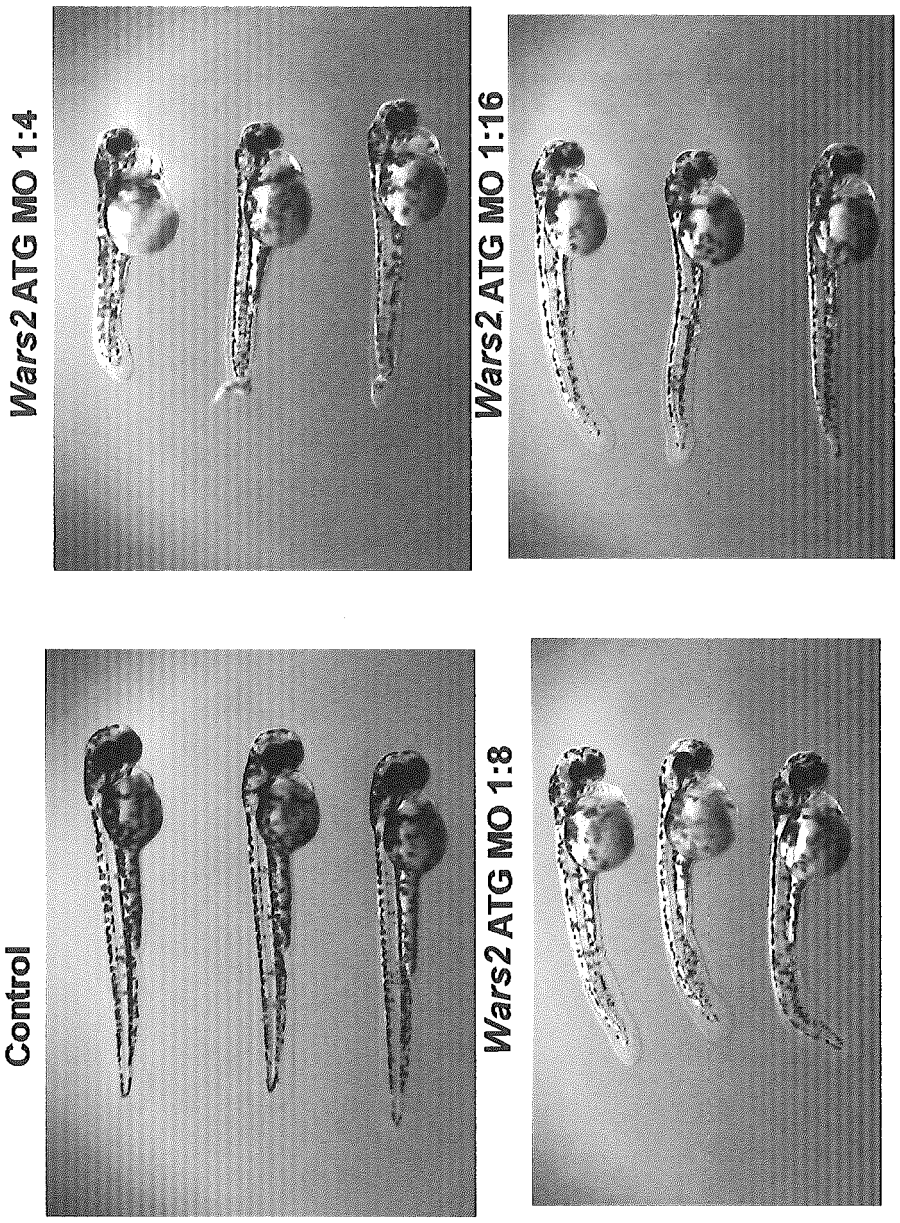


FIG. 10

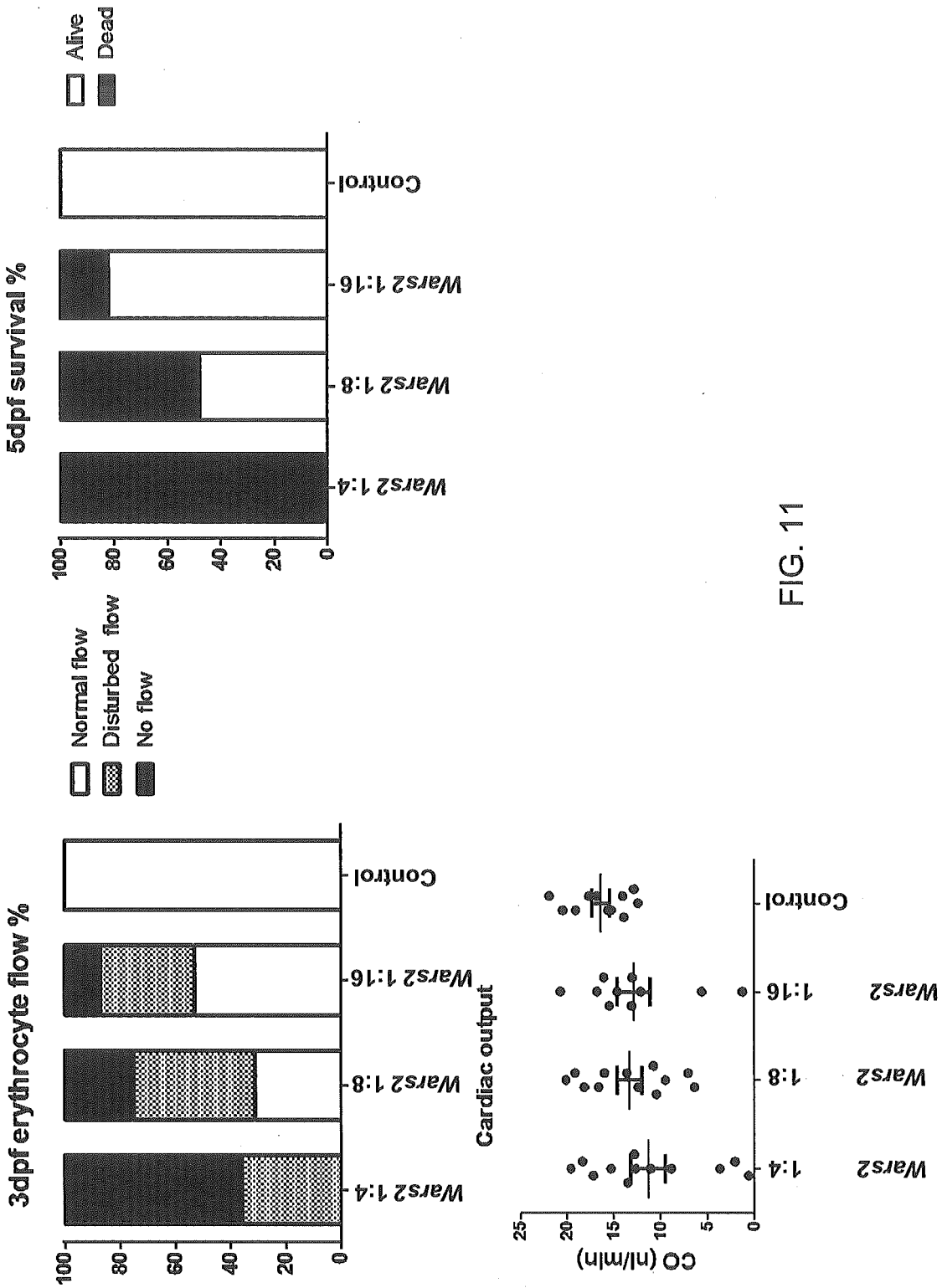

Alive
Dead
5dpf survival %
100
80
60
40
20
0
Wars2 1:4
Wars2 1:8
Wars2 1:16
Control
Normal flow
Disturbed flow
No flow
3dpf erythrocyte flow %
Cardiac output
CO (nl/min)
25
20
15
10
5
0
Wars2 1:4
Wars2 1:8
Wars2 1:16
Control

FIG. 11

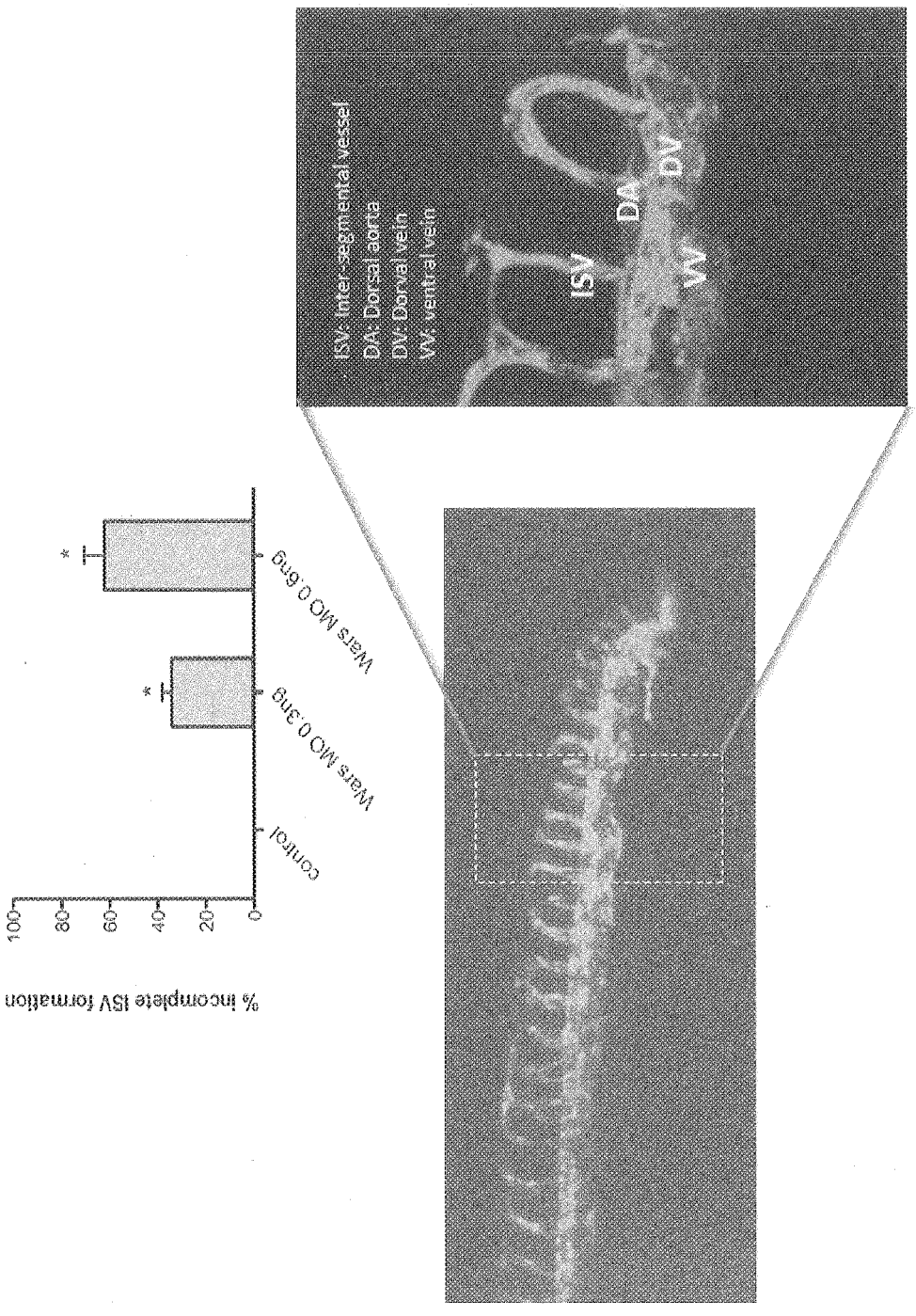

ISV: inter-segmental vessel
DA: Dorsal aorta
DV: Dorsal vein
VV: ventral vein
ISV
DA
DV
VV
% incomplete ISV formation
100
80
60
40
20
0
control
Wars MO 0.3ng
Wars MO 0.6ng
*
*

FIG. 12

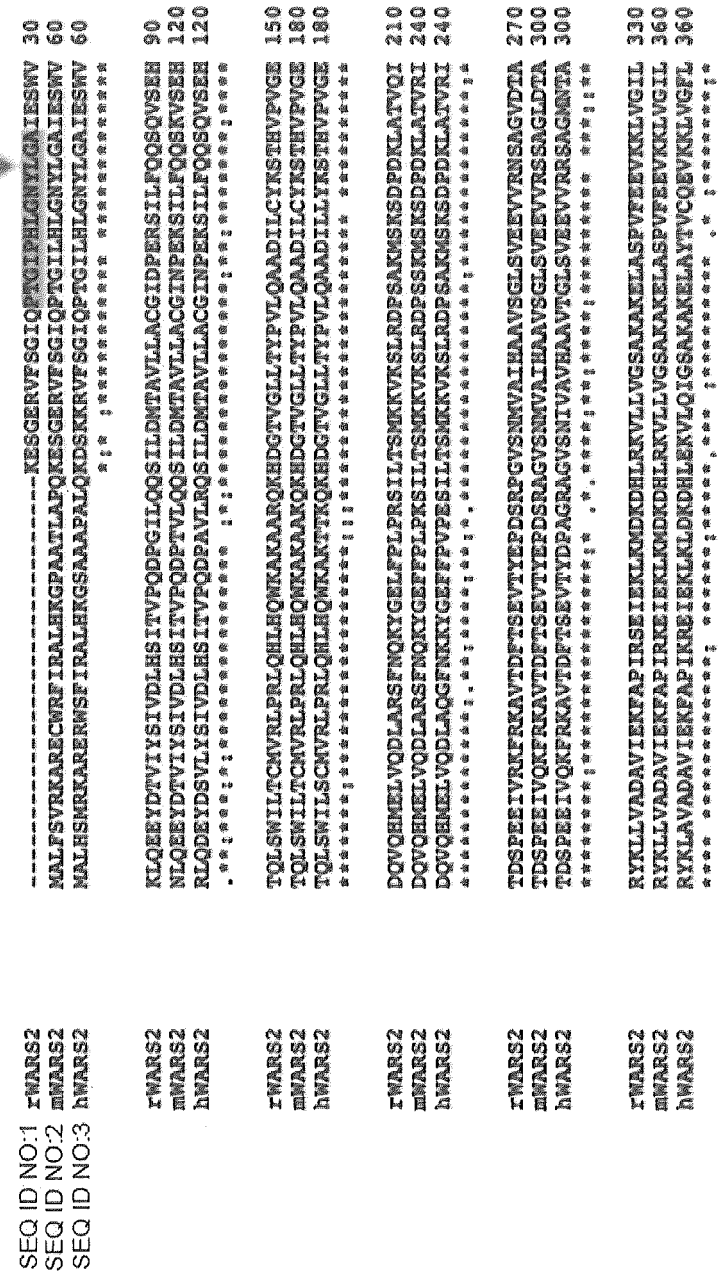

CLUSTAL 2.1 multiple sequence alignment
SEQ ID NO:1 rWARS2
SEQ ID NO:2 mWARS2
SEQ ID NO:3 hWARS2
rWARS2
mWARS2
hWARS2
rWARS2
mWARS2
hWARS2
rWARS2
mWARS2
hWARS2
rWARS2
mWARS2
hWARS2
rWARS2
mWARS2
hWARS2

FIG. 13

Human *WARS2* (SEQ ID NO:4)

ATGGCGCTGCACTCAATGCGGAAAGCGCGTGAGCGCTGGAGCTTCATCCGGGCACTTCAT
AAGGGATCCGCAGCTGCTCCCGCTCTCCAGAAAGACAGCAAGAAGCGAGTATTTTCCGGC
ATTCAACCTACAGGAATCCTCCACCTGGGCAATTACCTGGGAGCCATTGAGAGCTGGGTG
AGGTTACAGGATGAATATGACTCTGTATTATACAGCATTGTTGACCTCCACTCCATTACT
GTCCCCCAAGACCCAGCTGTCCTTCGGCAGAGCATCCTGGACATGACTGCTGTTCTTCTT
GCCTGTGGCATAAACCCGGAAAAAAAGCATCCTTTTCCAACAATCTCAGGTGTCTGAACAC
ACACAATTAAGTTGGATCCTTTCCTGCATGGTCAGACTACCTCGATTACAACATTTACAT
CAGTGGAAGGCAAAGACTACCAAGCAGAAGCACGATGGCACGGTGGGCCTGCTCACATAC
CCAGTACTCCAGGCAGCCGACATTCTGTTGTACAAGTCCACACACGTTCCTGTTGGGGAG
GATCAAGTCCAGCACATGGAACTAGTTCAGGATCTAGCACAAGGTTTCAACAAGAAGTAT
GGGGAGTTCTTTCCAGTGCCCGAGTCCATTCTCACATCCATGAAGAAGGTAAAATCCCTA
CGTGATCCTTCTGCCAAAATGTCGAAATCAGACCCTGACAAACTGGCCACCGTCCGAATA
ACAGACAGCCCAGAGGAGATAGTGCAGAAATTCCGCAAGGCTGTGACAGACTTCACCTCG
GAGGTCACCTATGACCCGGCTGGCCGCGCTGGCGTGTCCAACATAGTGGCGGTGCATGCC
GCGGTGACGGGGCTCTCCGTGGAGGAAGTGGTGCGCCGCAGCGCGGGCATGAACACTGCT
CGCTACAAGCTGGCCGTGGCAGATGCTGTGATTGAGAAGTTTGCCCCAATTAAGCGTGAA
ATTGAAAAACTGAAGCTGGACAAGGACCATTTAGAGAAGGTTTTACAAATTGGATCAGCA
AAAGCCAAAGAATTAGCATACACTGTGTGCCAGGAGGTGAAGAAATTGGTGGGTTTTCTA
TAG

FIG. 14

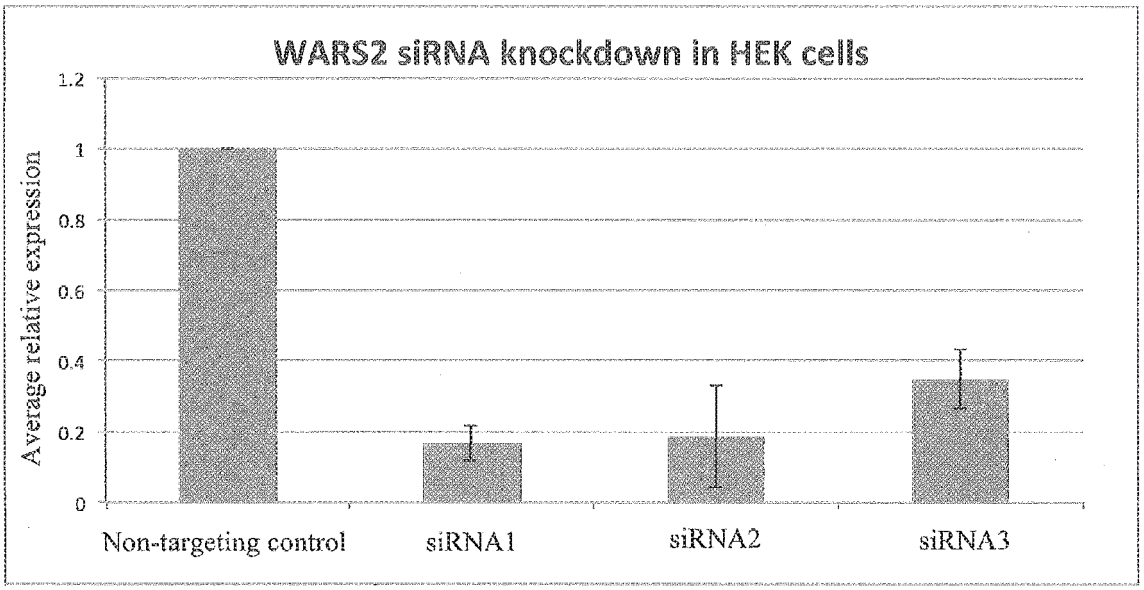

WARS2 siRNA knockdown in HEK cells
Average relative expression
1.2
1
0.8
0.6
0.4
0.2
0
Non-targeting control
siRNA1
siRNA2
siRNA3

FIG. 15

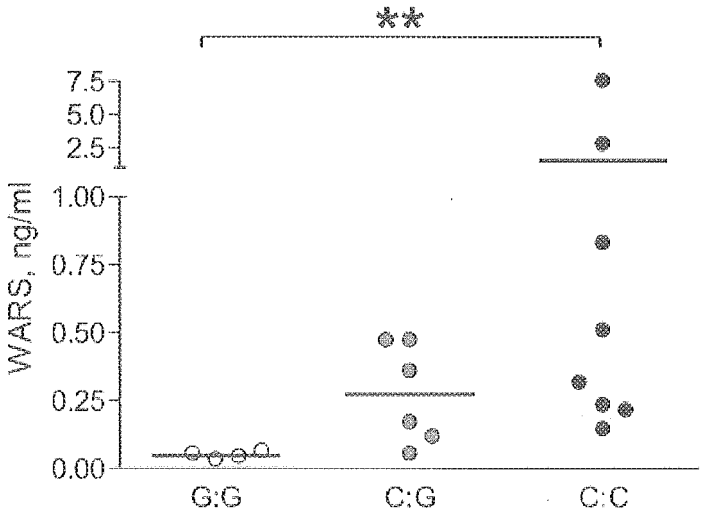

**
WARS, ng/ml
7.5
5.0
2.5
1.00
0.75
0.50
0.25
0.00
G:G
C:G
C:C

FIG. 16

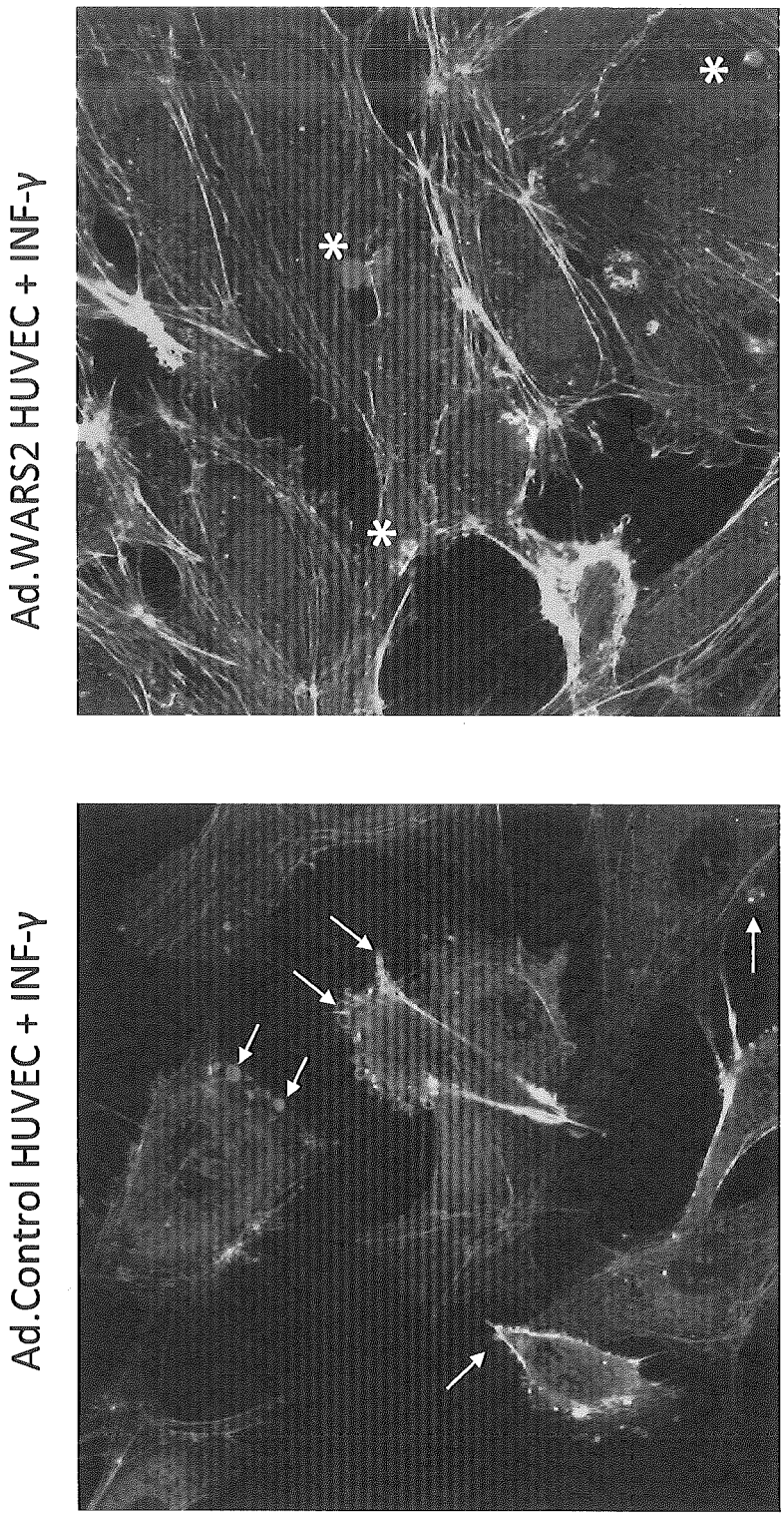
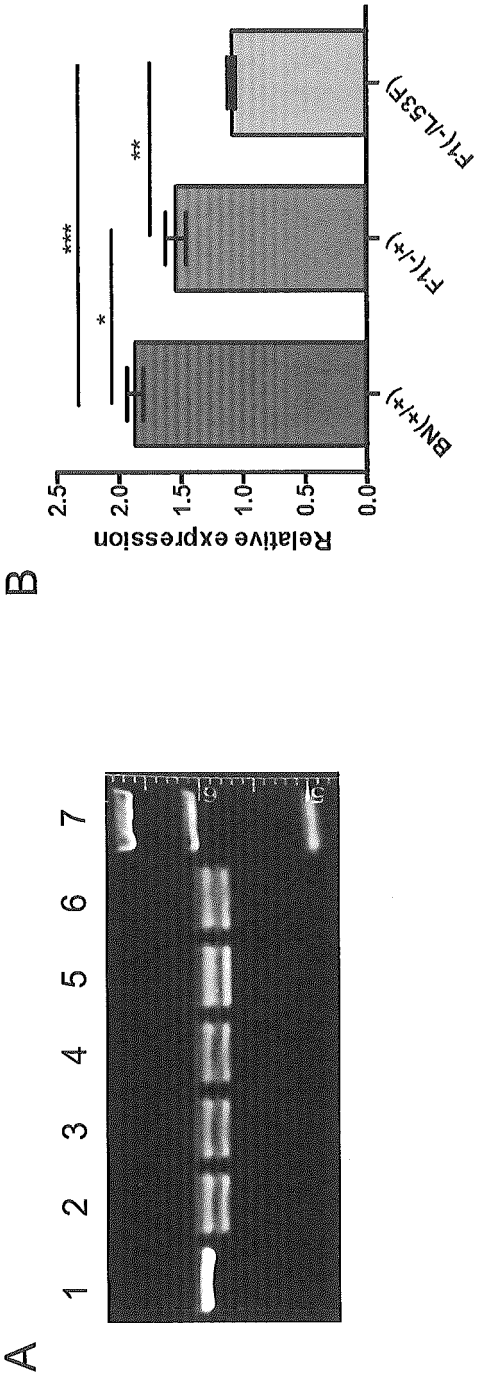
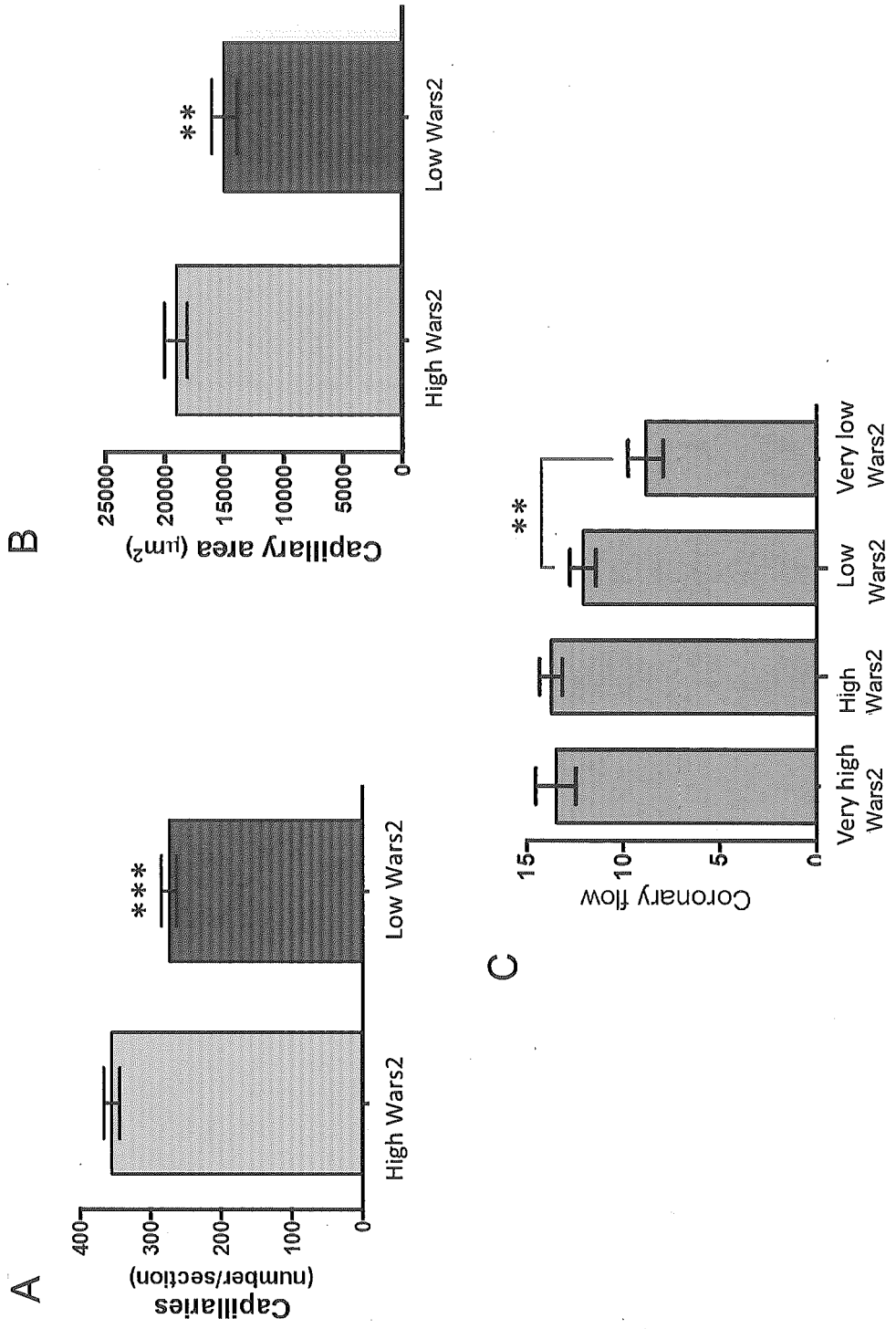


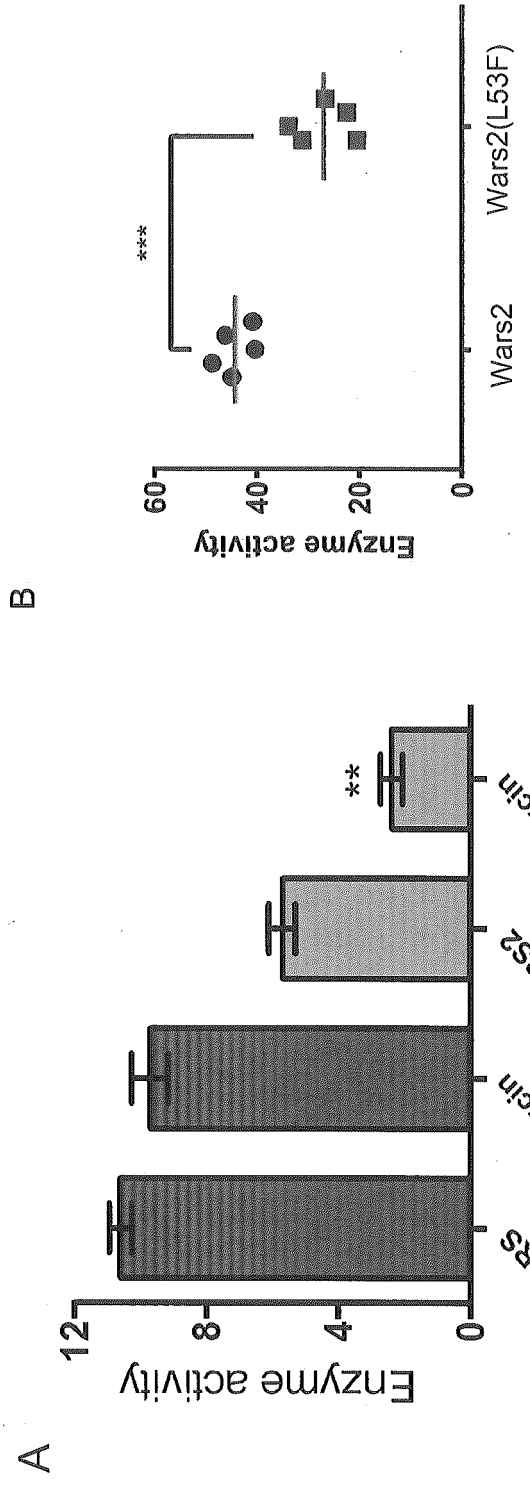
FIG. 17



FIGS. 18A-B


A
Capillaries (number/section)
400
300
200
100
0
***
High Wars2
Low Wars2
B
Capillary area (μm²)
25000
20000
15000
10000
5000
0
**
High Wars2
Low Wars2
C
Coronary flow
15
10
5
0
**
Very high Wars2
High Wars2
Low Wars2
Very low Wars2

FIGS. 19A-C


A
Enzyme activity
0
4
8
12
WARS
WARS + Indolmycin
WARS2
WARS2 + Indolmycin
**
B
Enzyme activity
0
20
40
60
***
Wars2
Wars2(L53F)

FIGS. 20A-B

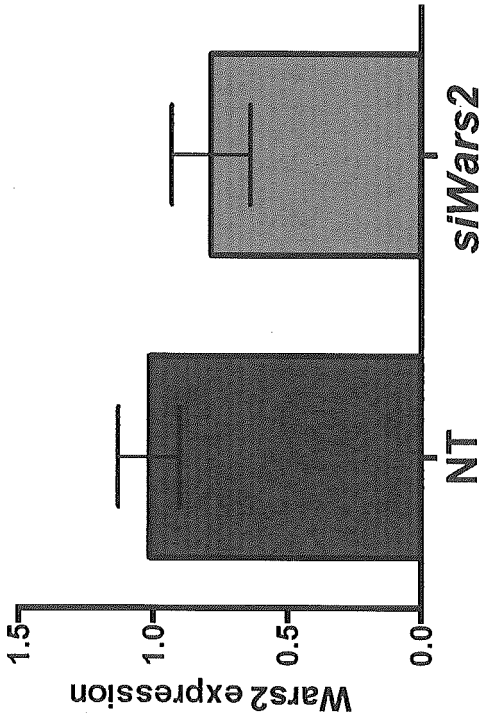
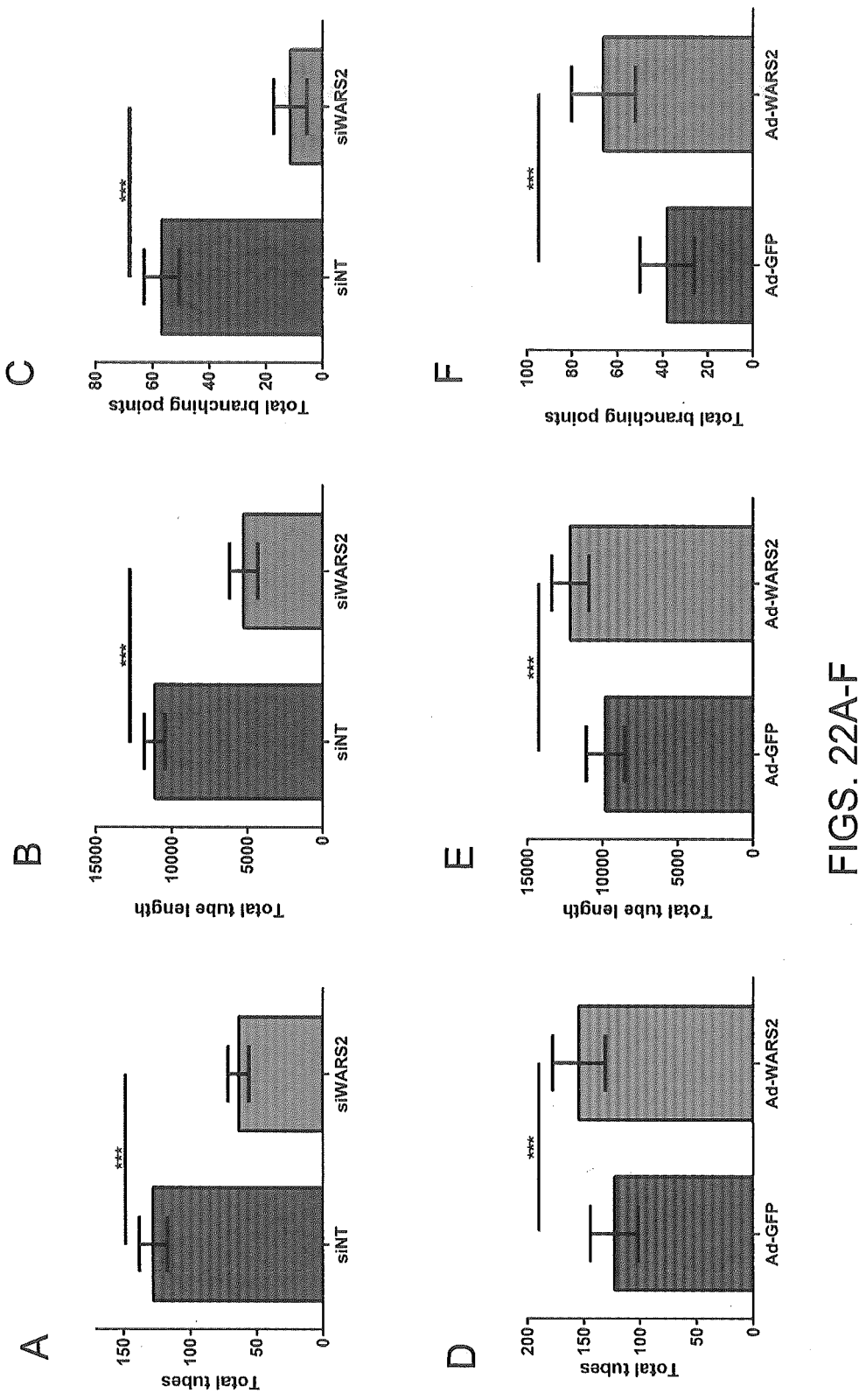


FIG. 21


A
Total tubes
150
100
50
0
***
siNT
siWARS2
B
Total tube length
15000
10000
5000
0
***
siNT
siWARS2
C
Total branching points
80
60
40
20
0
***
siNT
siWARS2
D
Total tubes
200
150
100
50
0
***
Ad-GFP
Ad-WARS2
E
Total tube length
15000
10000
5000
0
***
Ad-GFP
Ad-WARS2
F
Total branching points
100
80
60
40
20
0
***
Ad-GFP
Ad-WARS2

FIGS. 22A-F

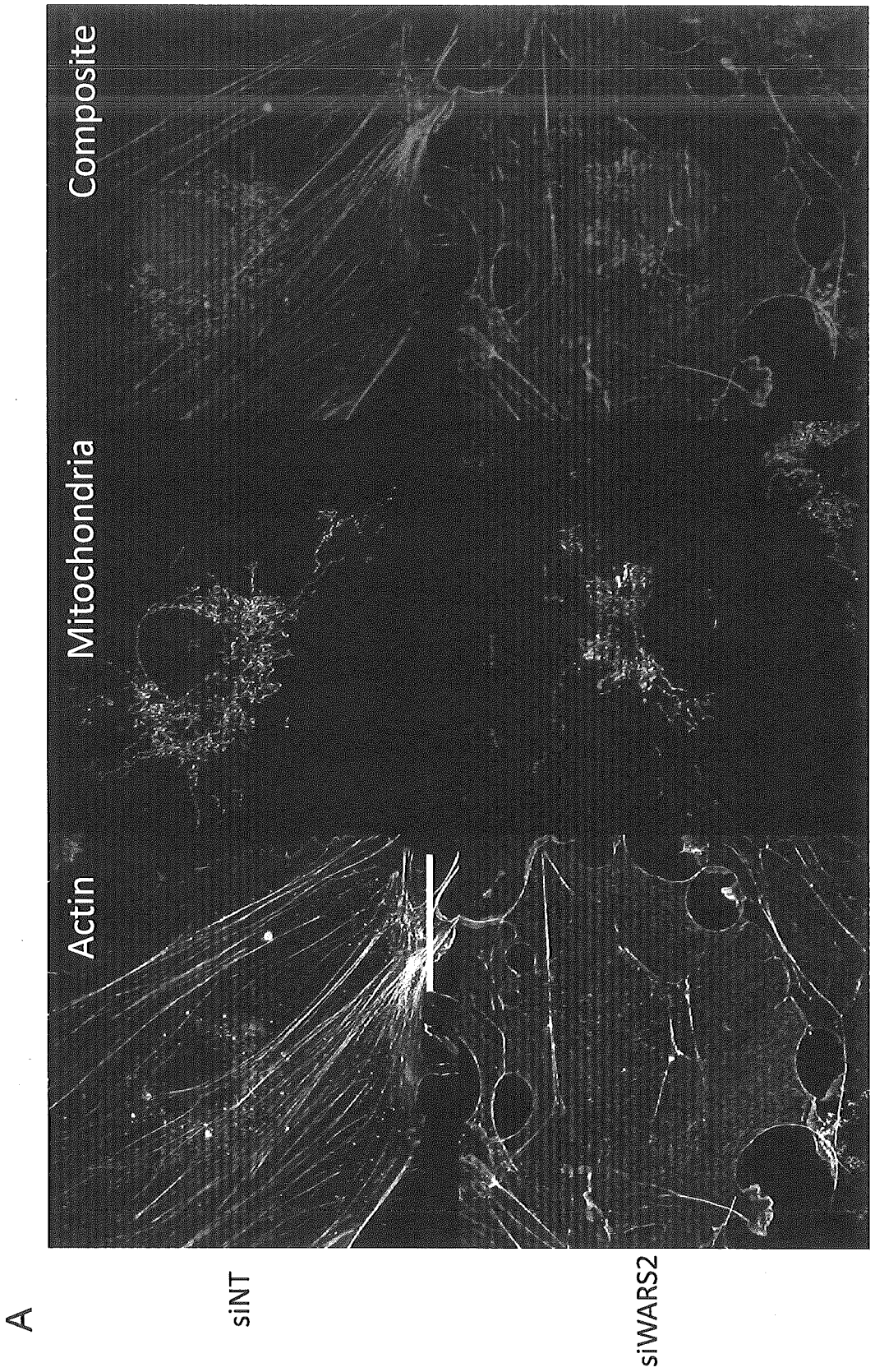


FIG. 23A

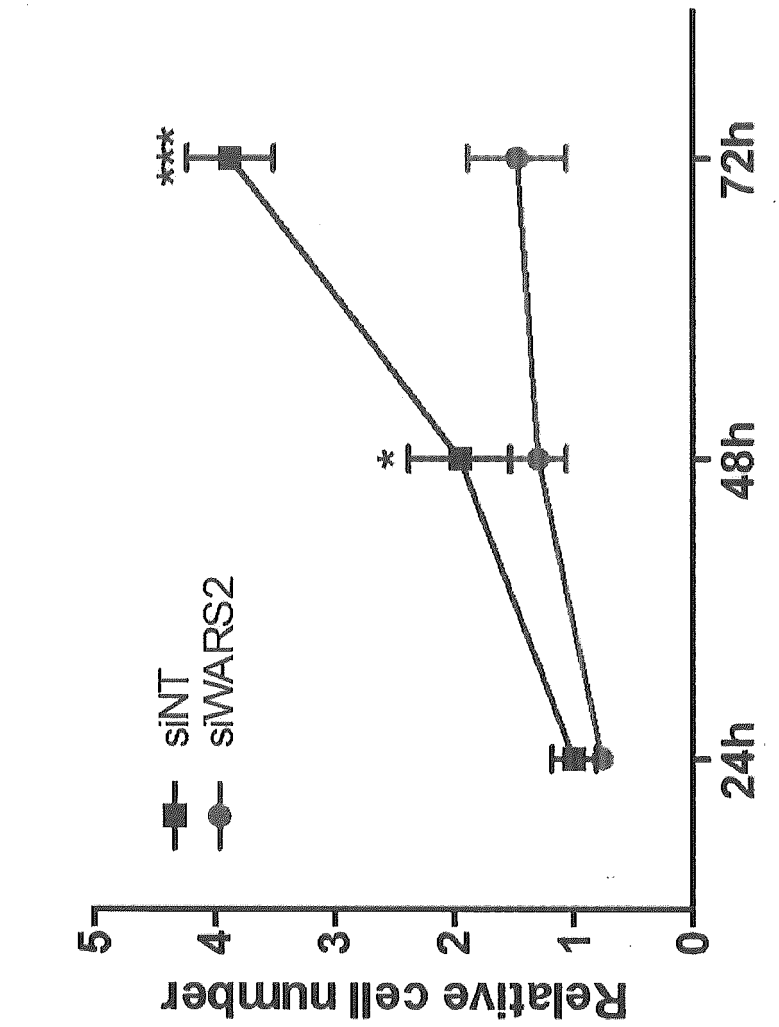
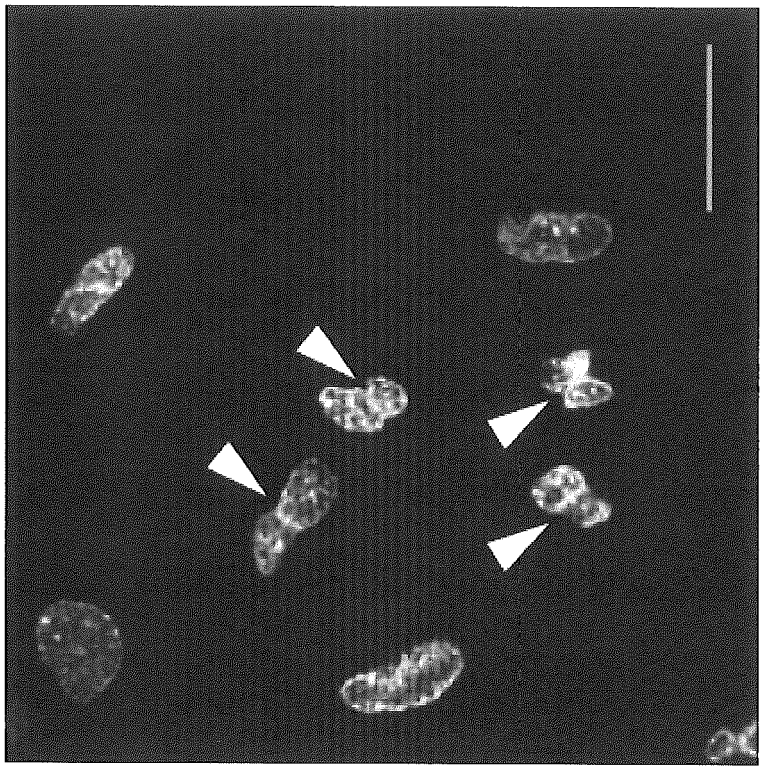


FIG. 23B



A

FIG. 24A

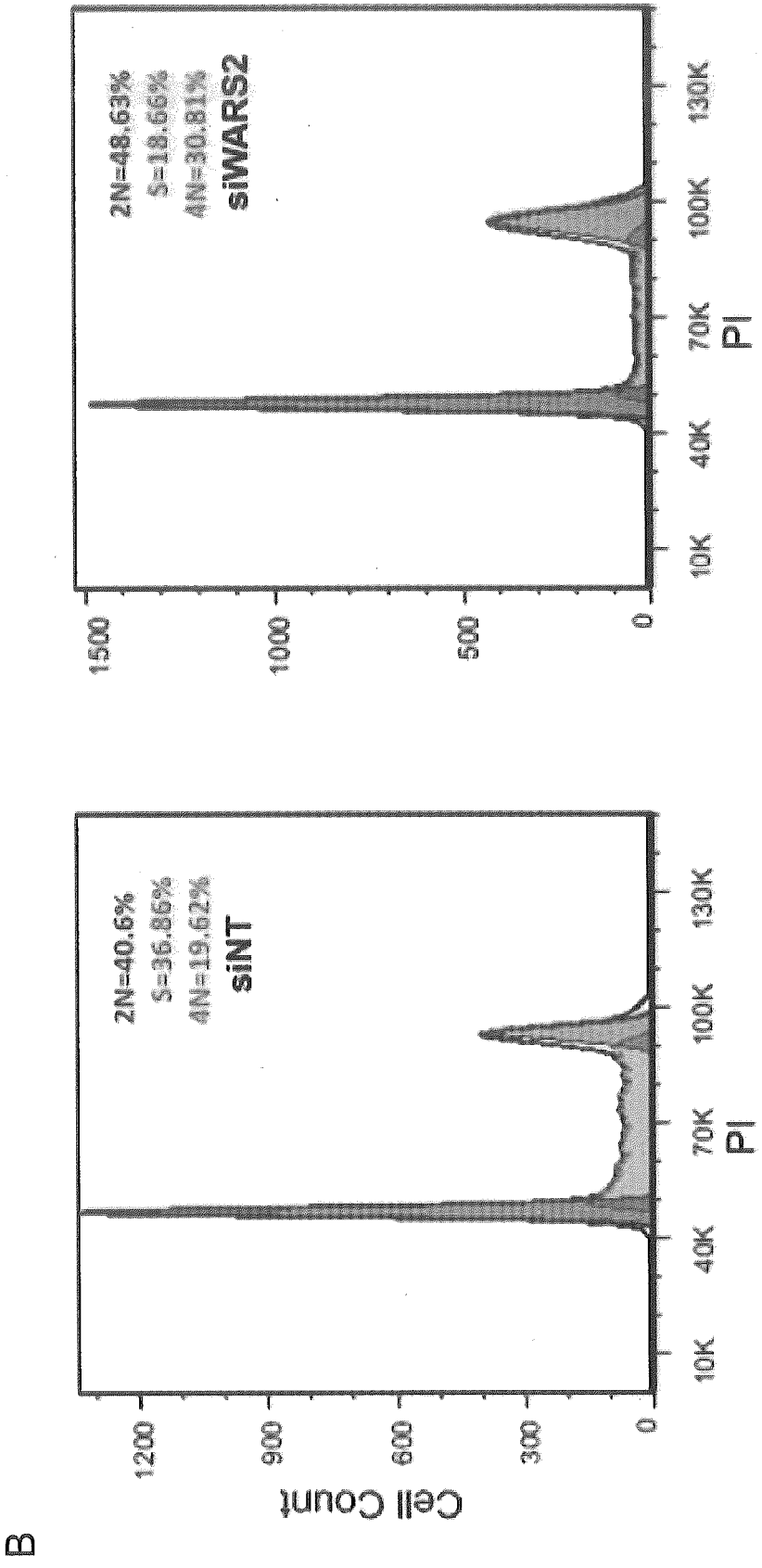

B
Cell Count
1200
900
600
300
0
10K
40K
70K
100K
130K
PI
2N=40.6%
S=36.86%
4N=19.62%
siNT
1500
1000
500
0
10K
40K
70K
100K
130K
PI
2N=48.63%
S=18.66%
4N=30.81%
siWARS2

FIG. 24B

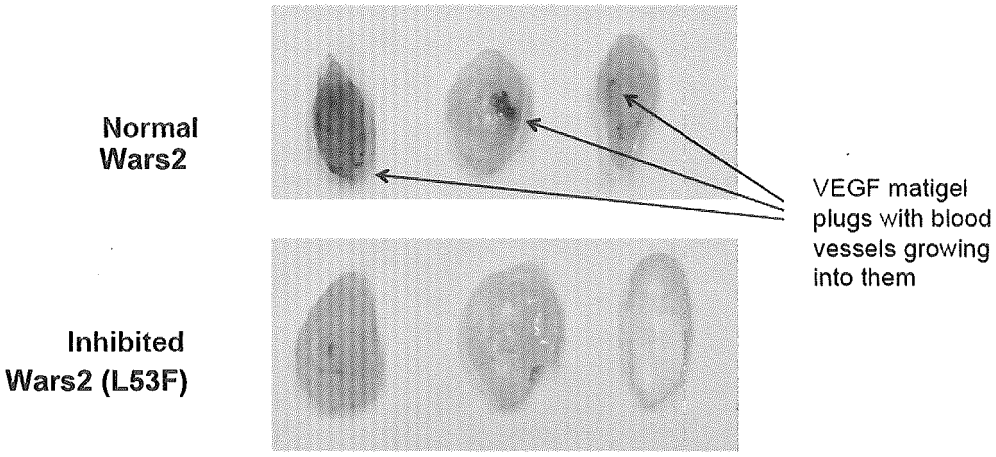

Normal
Wars2
Inhibited
Wars2 (L53F)
VEGF matigel
plugs with blood
vessels growing
into them

FIG. 25

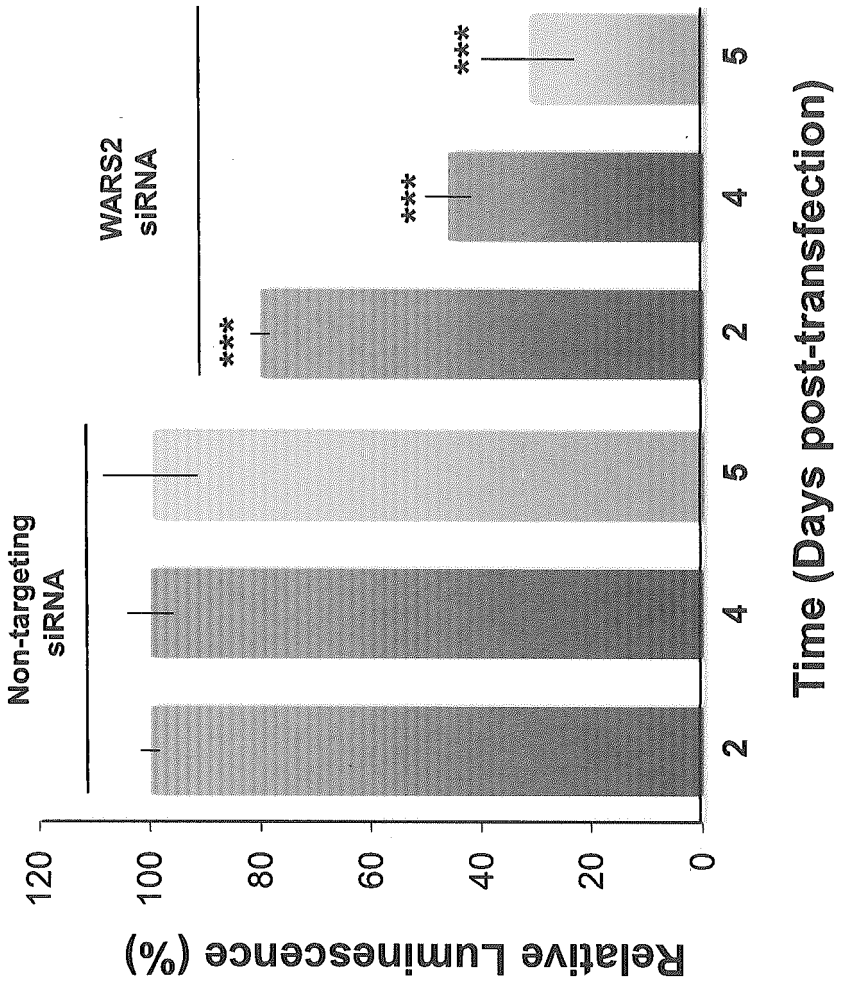

Relative Luminescence (%)
120
100
80
60
40
20
0
Non-targeting siRNA
WARS2 siRNA
***
***
***
2
4
5
2
4
5
Time (Days post-transfection)

FIG. 26