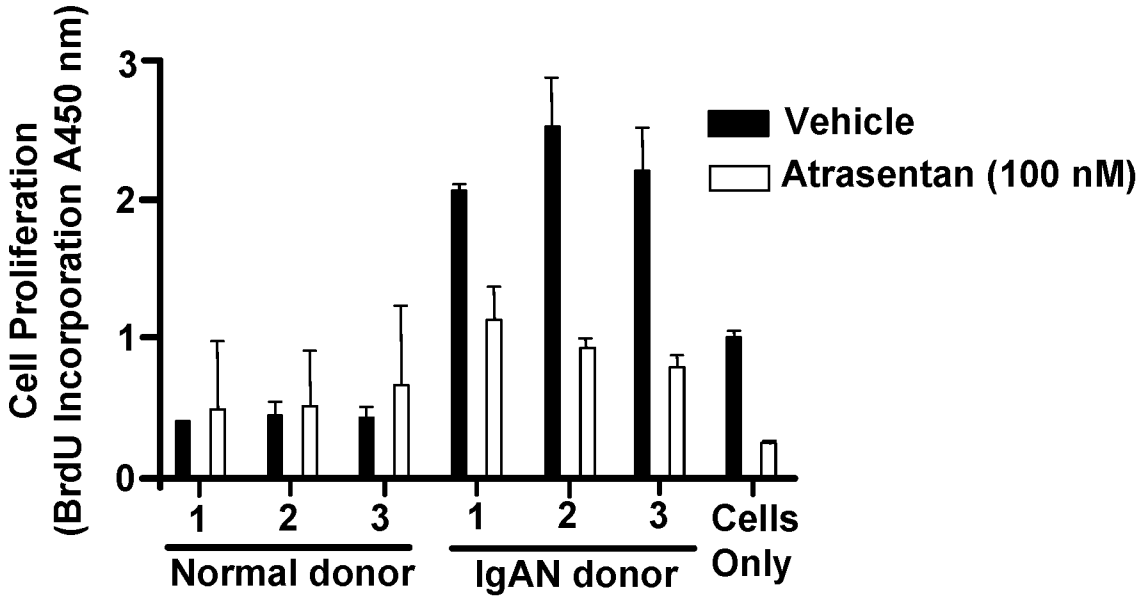

Cell Proliferation
(BrdU Incorporation A450 nm)
3
2
1
0
Vehicle
Atrasentan (100 nM)
1
2
3
1
2
3
Cells
Only
Normal donor
IgAN donor

FIG. 1A

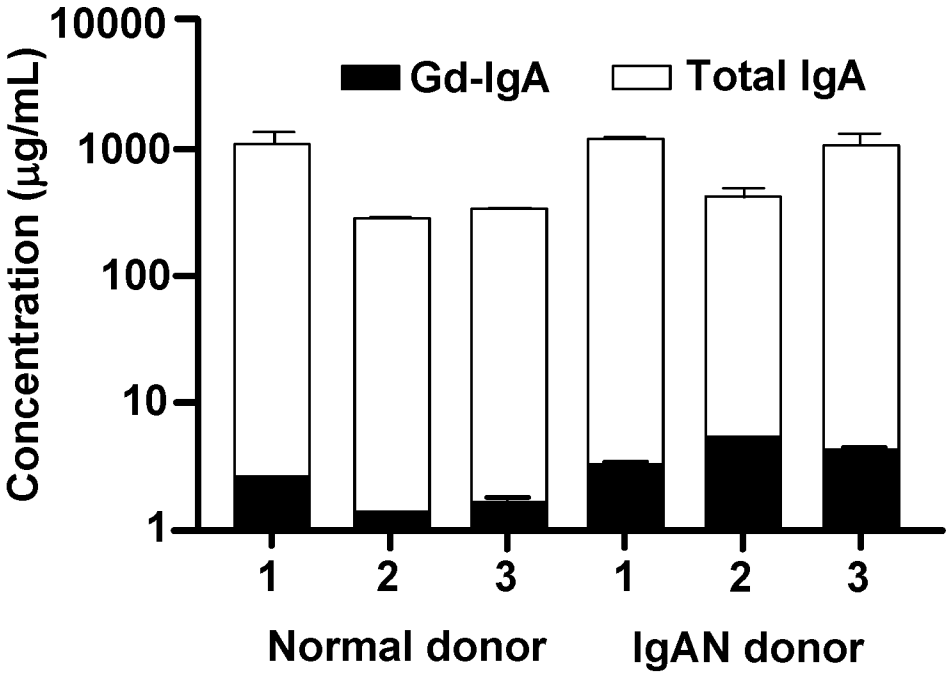

Concentration (µg/mL)
10000
1000
100
10
1
Gd-IgA
Total IgA
1
2
3
1
2
3
Normal donor
IgAN donor

FIG. 1B

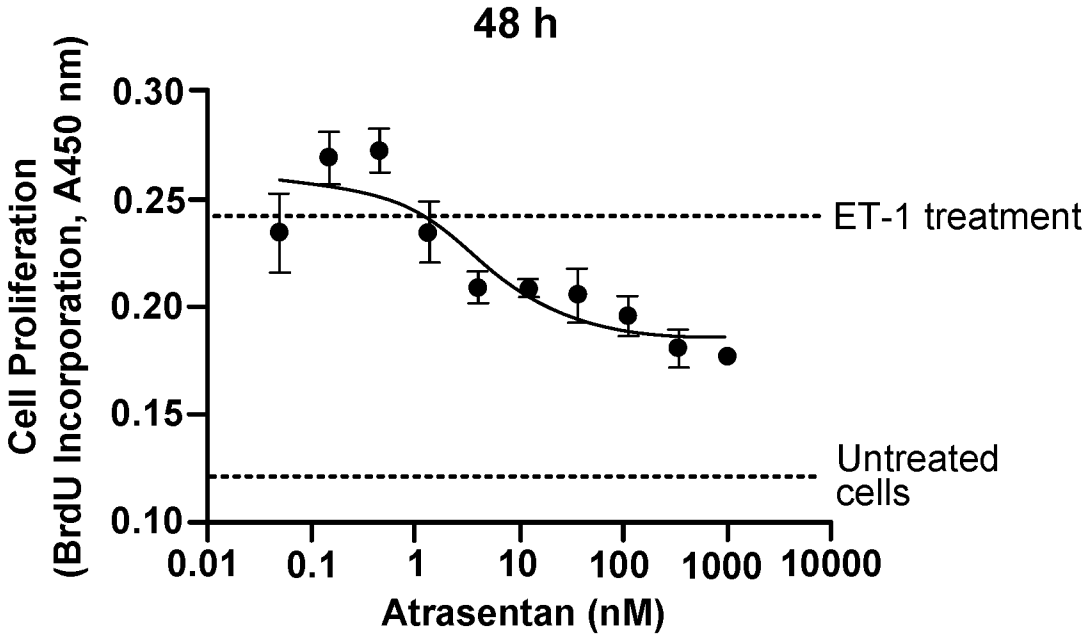

48 h
Cell Proliferation
(BrdU Incorporation, A450 nm)
0.30
0.25
0.20
0.15
0.10
ET-1 treatment
Untreated
cells
0.01
0.1
1
10
100
1000
10000
Atrasentan (nM)

FIG. 2A

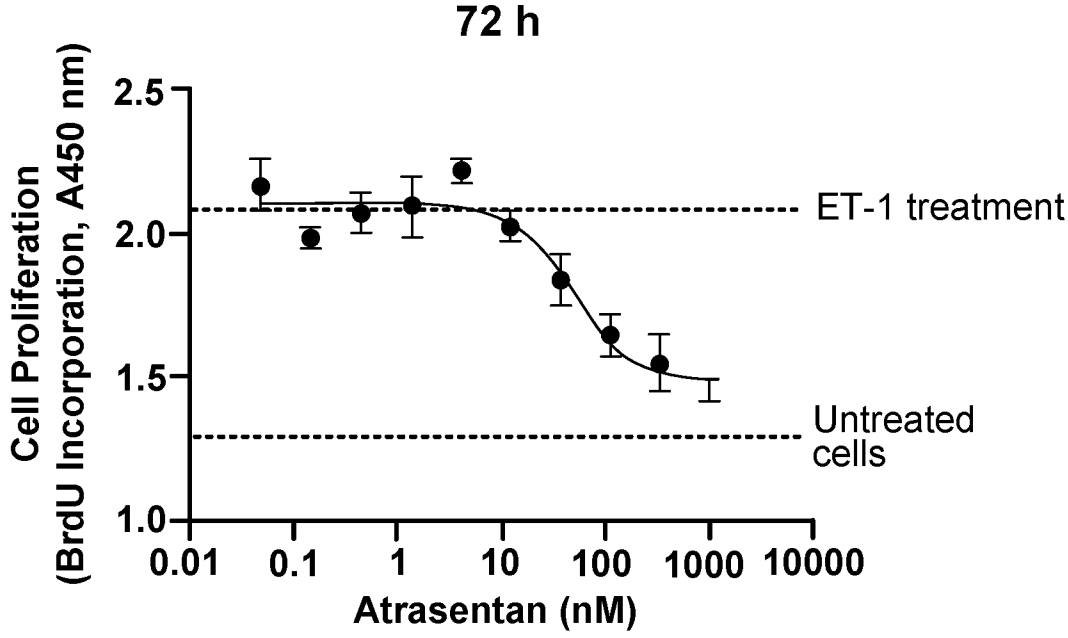

72 h
Cell Proliferation
(BrdU Incorporation, A450 nm)
2.5
2.0
1.5
1.0
ET-1 treatment
Untreated
cells
0.01
0.1
1
10
100
1000
10000
Atrasentan (nM)

FIG. 2B

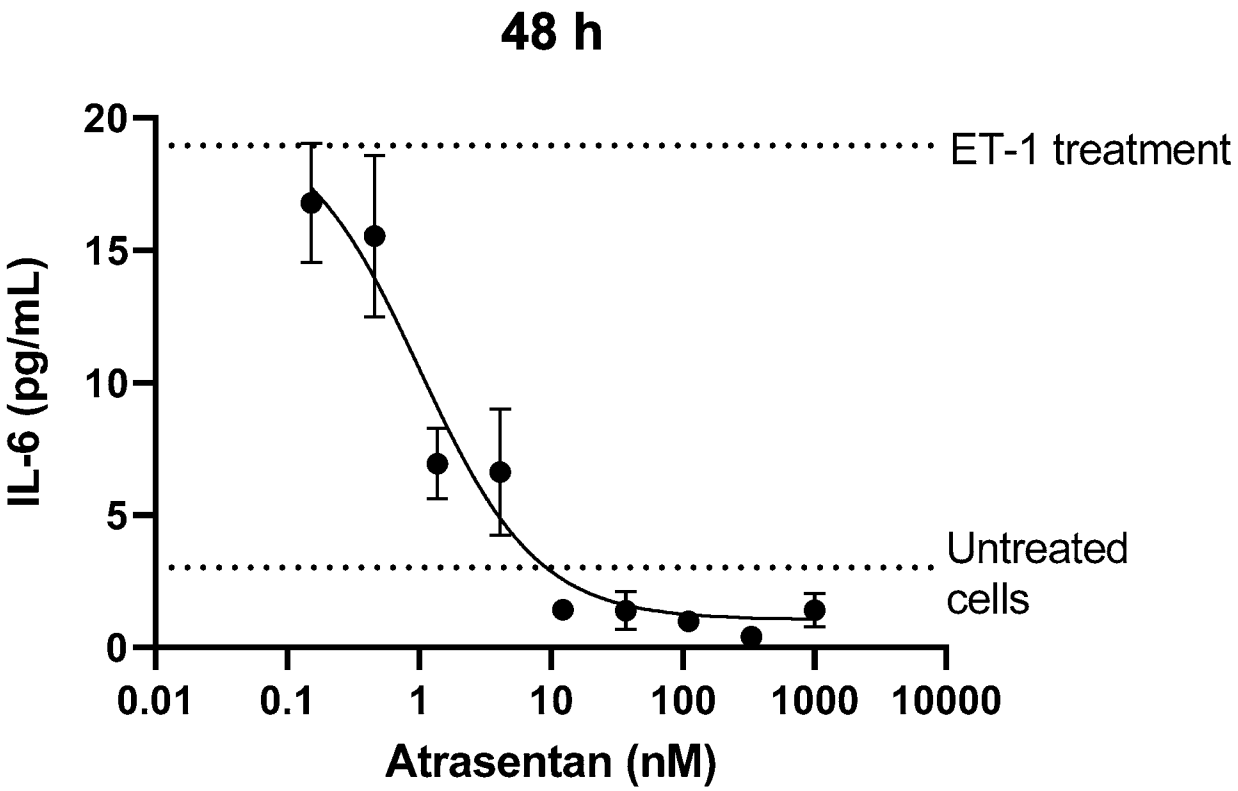

48 h
20
15
10
5
0
IL-6 (pg/mL)
ET-1 treatment
Untreated
cells
0.01
0.1
1
10
100
1000
10000
Atrasentan (nM)

FIG. 3A

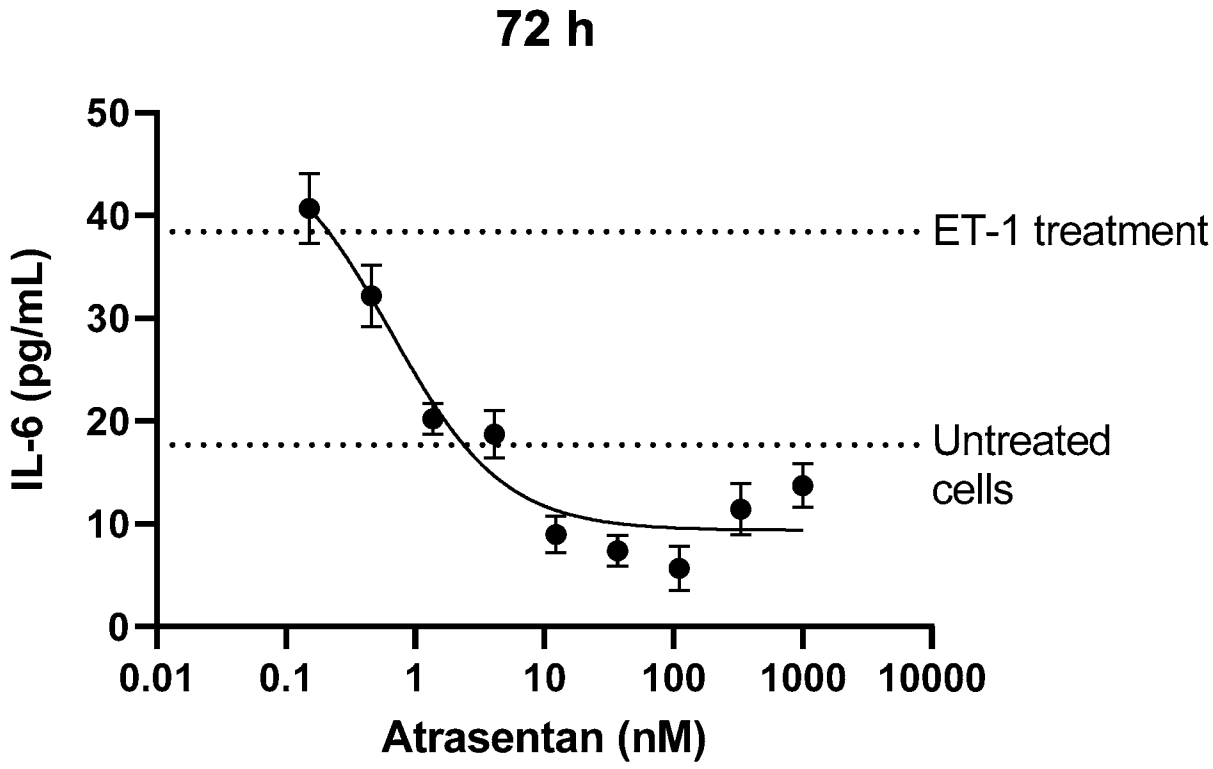

72 h
50
40
30
20
10
0
IL-6 (pg/mL)
ET-1 treatment
Untreated
cells
0.01
0.1
1
10
100
1000
10000
Atrasentan (nM)

FIG. 3B

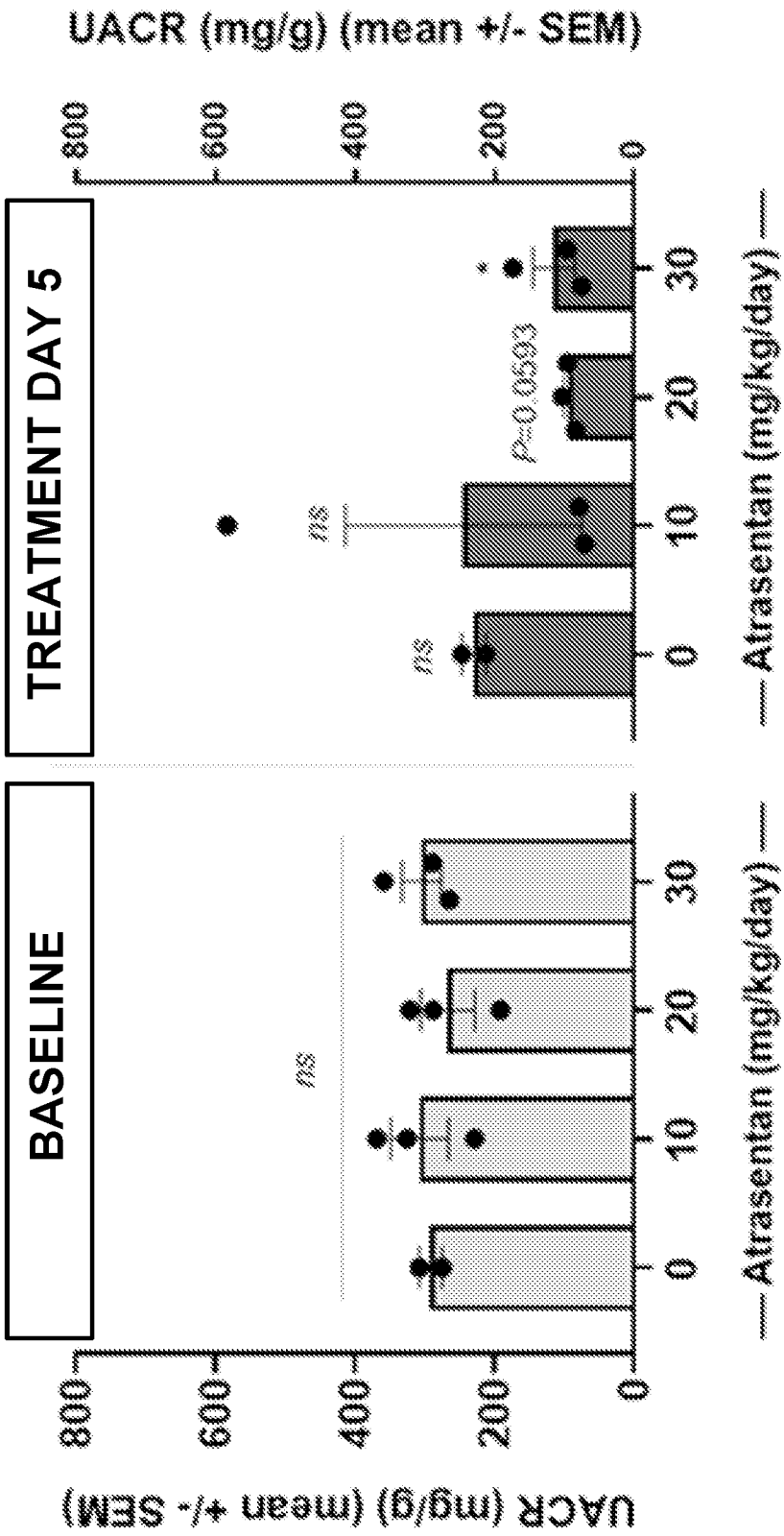

UACR (mg/g) (mean +/- SEM)
800
600
400
200
0
TREATMENT DAY 5
BASELINE
ns
ns
ns
P=0.0593
*
0
10
20
30
— Atrasentan (mg/kg/day) —
— Atrasentan (mg/kg/day) —

FIG. 4

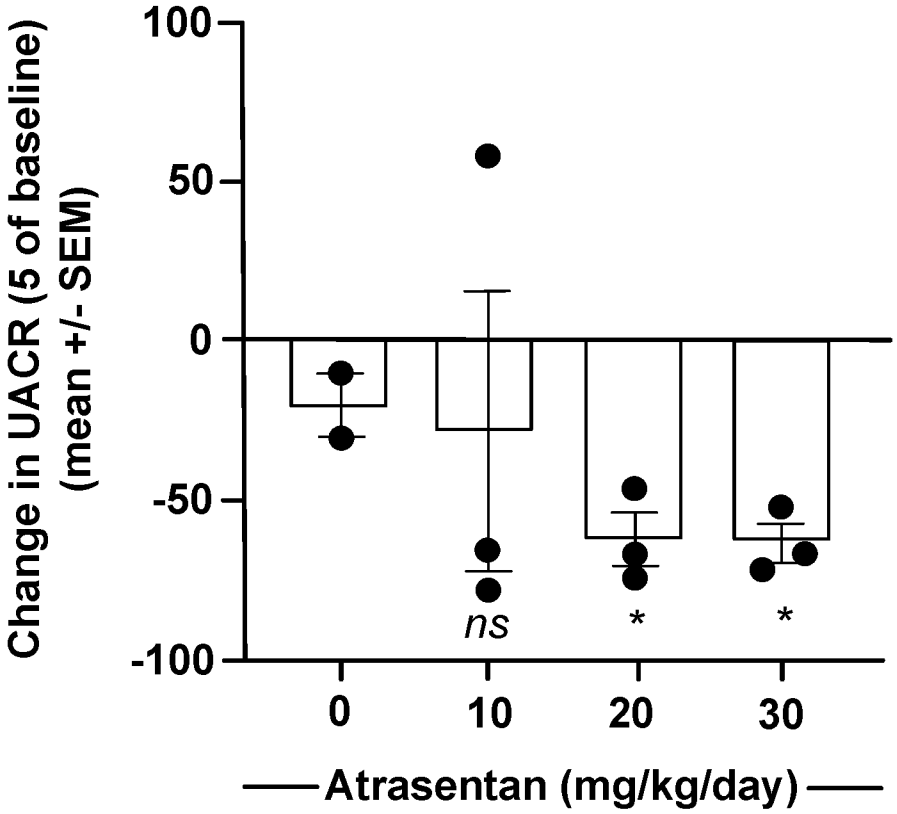

Change in UACR (5 of baseline)
(mean +/- SEM)
100
50
0
-50
-100
ns
*
*
0
10
20
30
Atrasentan (mg/kg/day)

FIG. 5

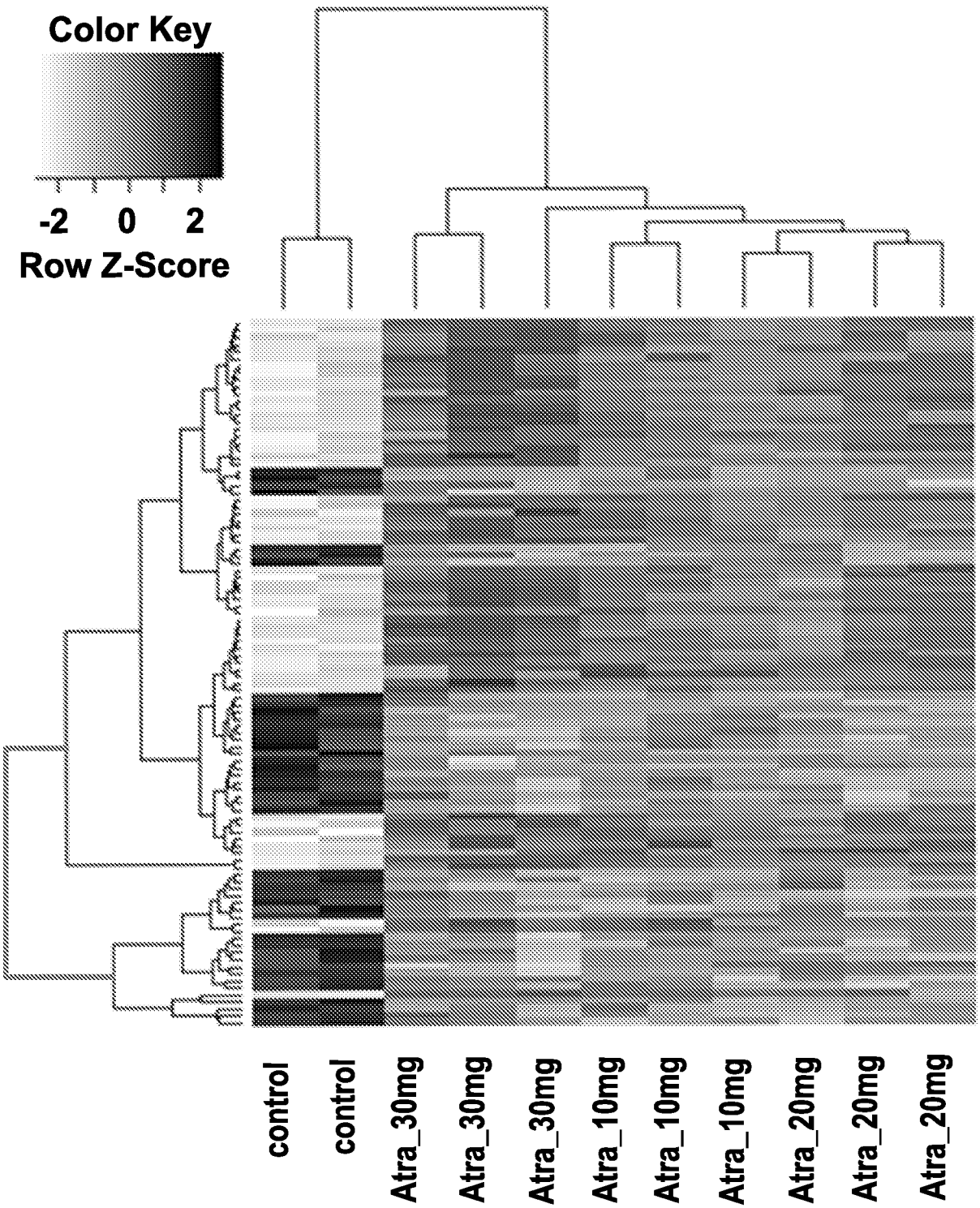

Color Key
-2
0
2
Row Z-Score
control
control
Atra_30mg
Atra_30mg
Atra_30mg
Atra_10mg
Atra_10mg
Atra_10mg
Atra_20mg
Atra_20mg
Atra_20mg

FIG. 6

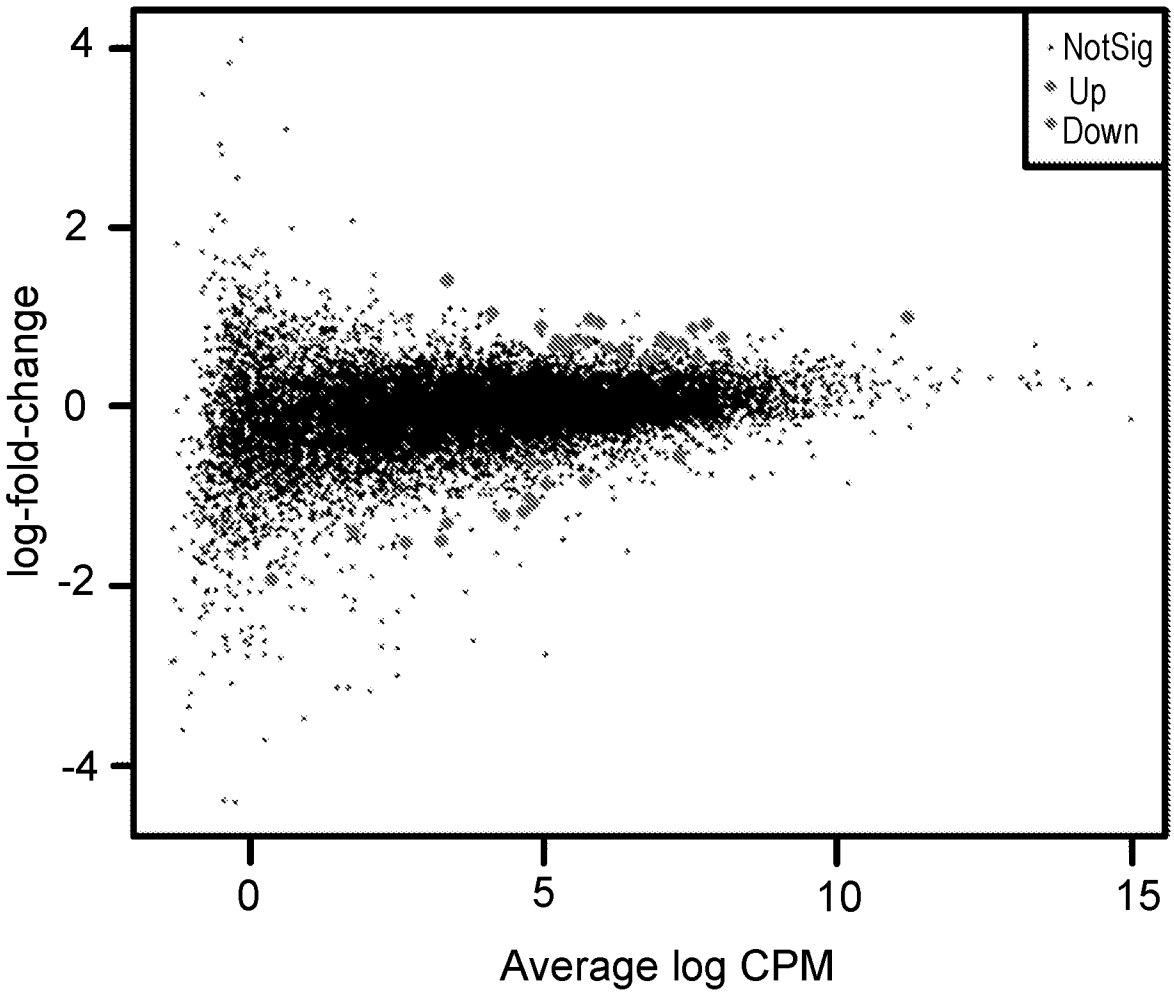


FIG. 7A

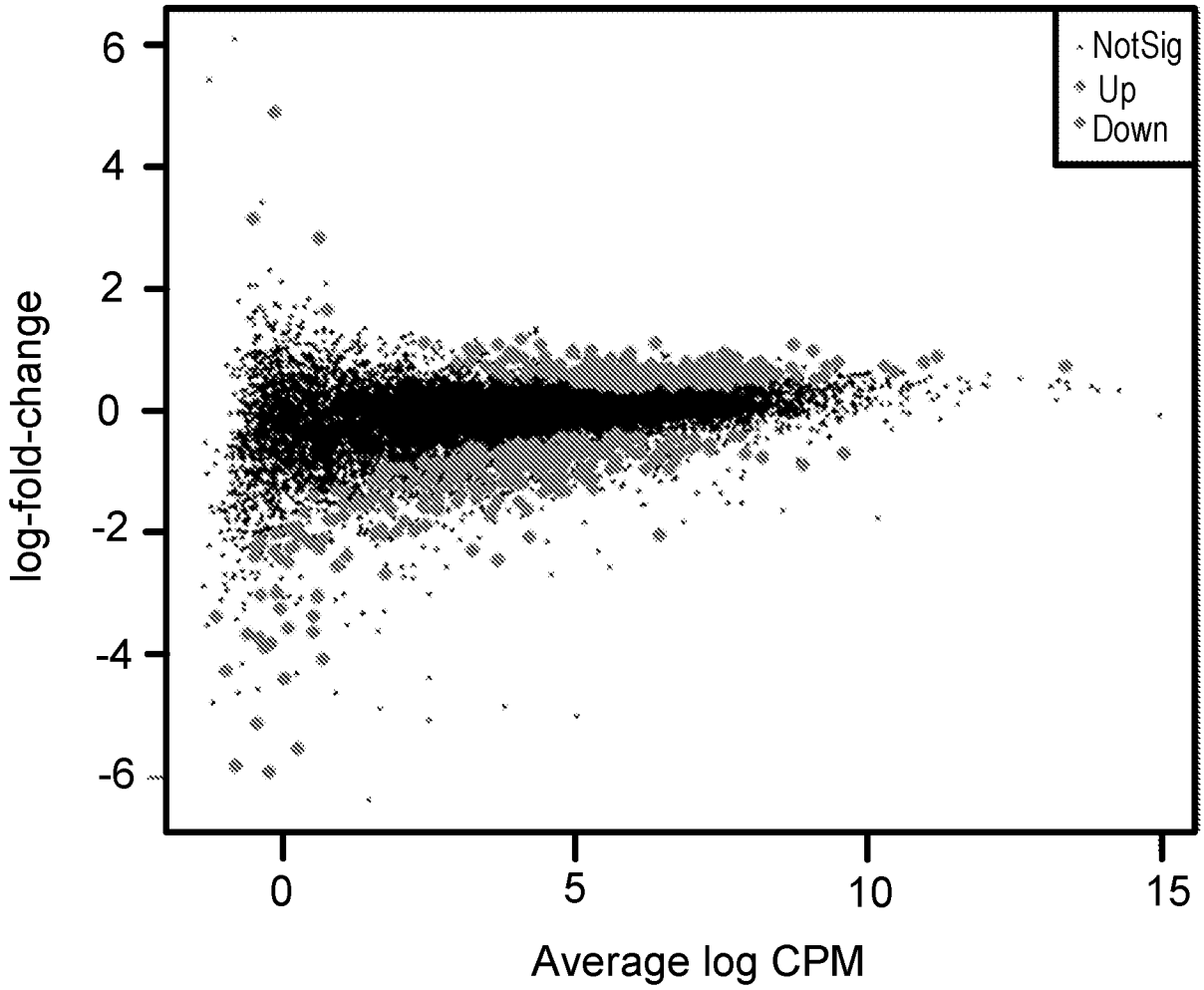

NotSig
Up
Down
log-fold-change
6
4
2
0
-2
-4
-6
0
5
10
15
Average log CPM

FIG. 7B

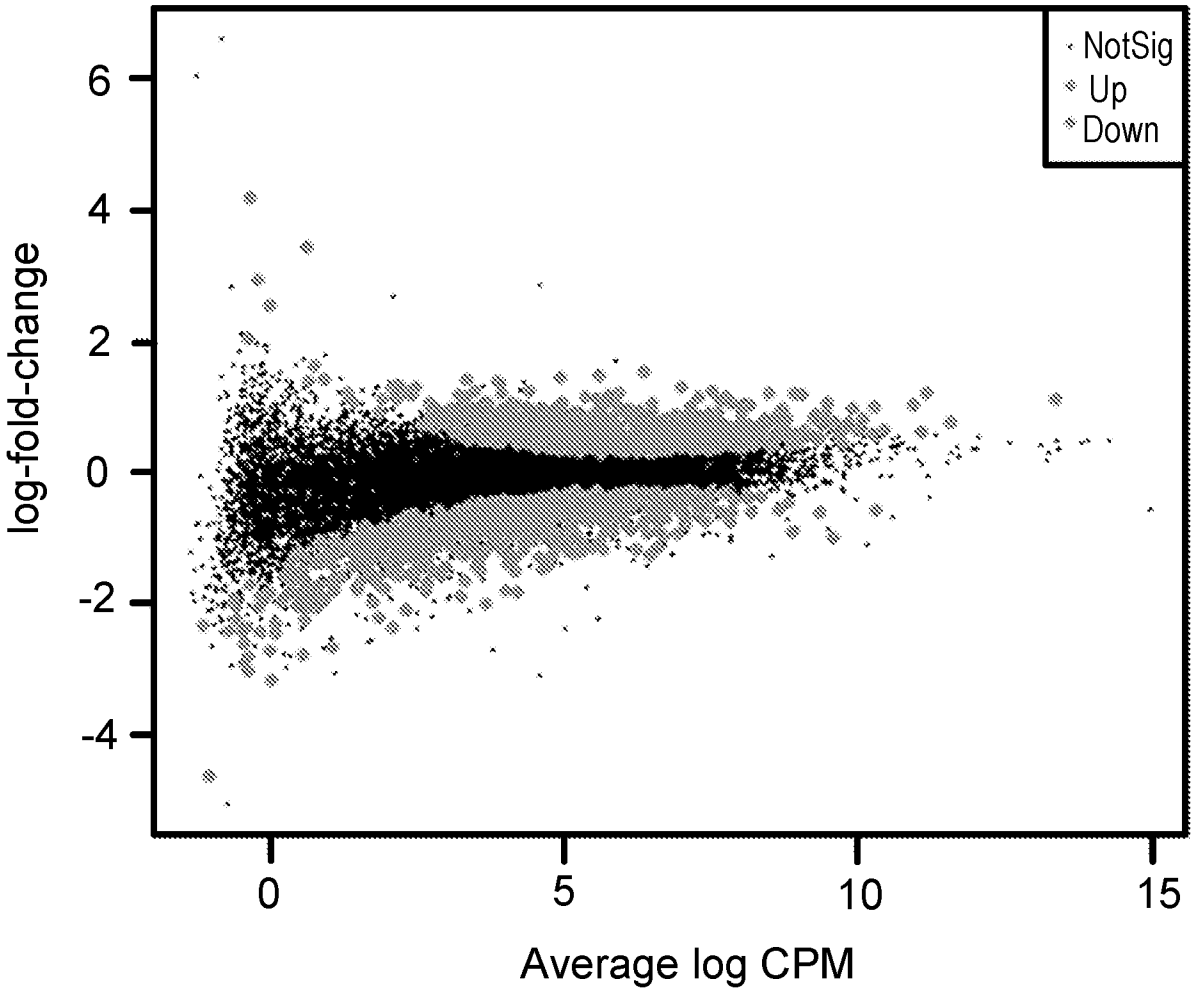

NotSig
Up
Down
log-fold-change
6
4
2
0
-2
-4
0
5
10
15
Average log CPM

FIG. 7C

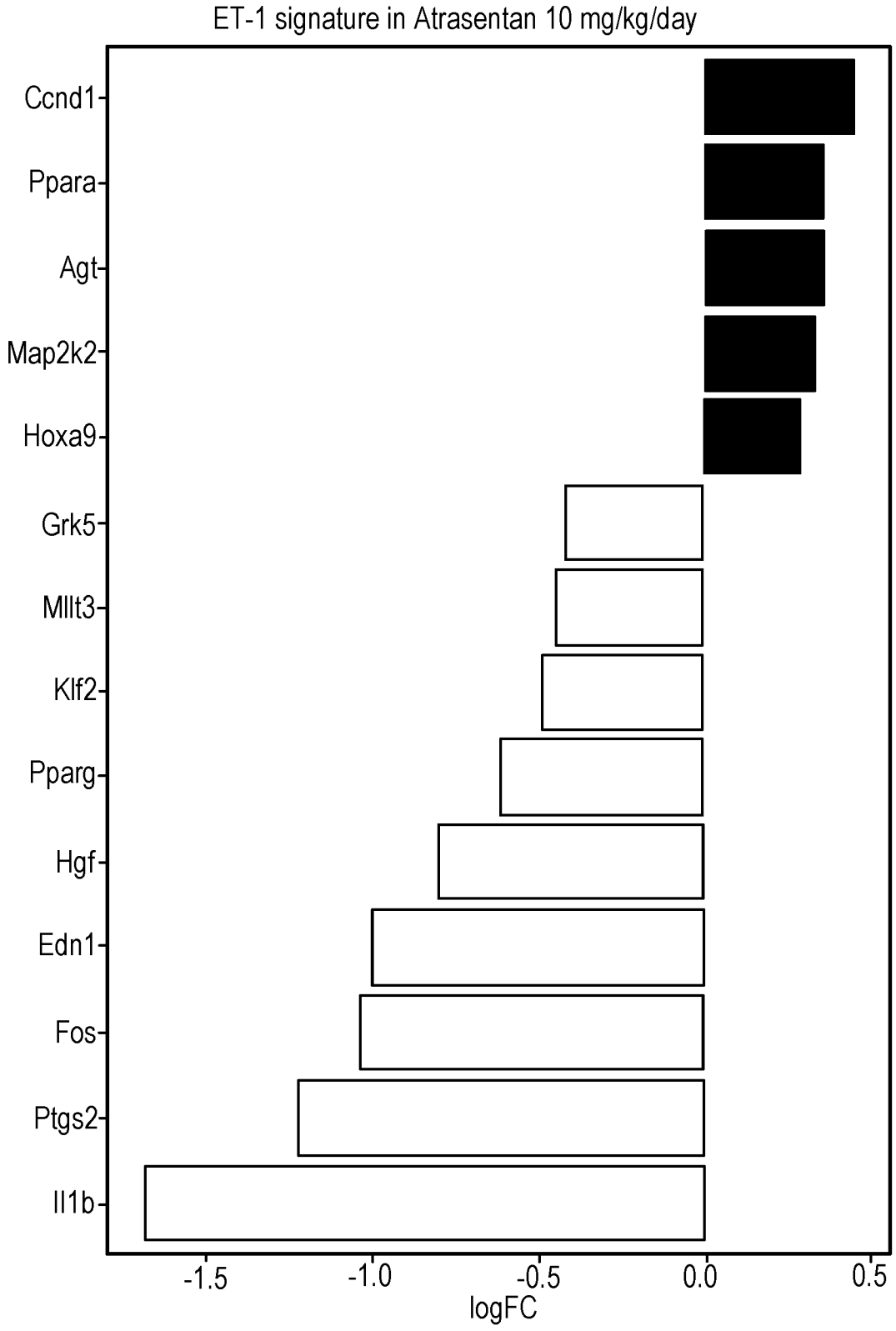

ET-1 signature in Atrasentan 10 mg/kg/day
Ccnd1
Ppara
Agt
Map2k2
Hoxa9
Grk5
Mllt3
Klf2
Pparg
Hgf
Edn1
Fos
Ptgs2
Il1b
-1.5
-1.0
-0.5
0.0
0.5
logFC

FIG. 8A

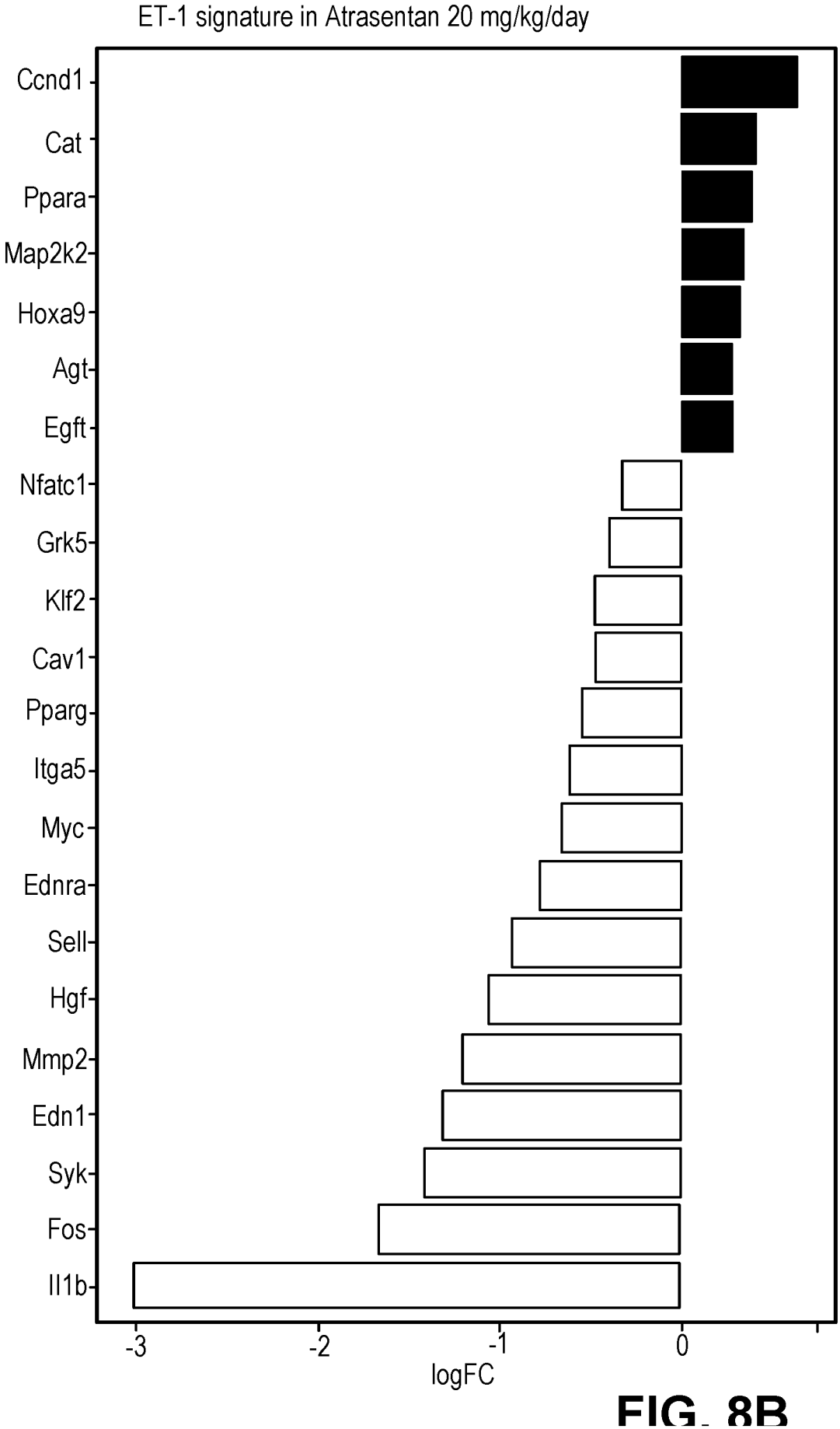

ET-1 signature in Atrasentan 20 mg/kg/day
Ccnd1
Cat
Ppara
Map2k2
Hoxa9
Agt
Egft
Nfatc1
Grk5
Klf2
Cav1
Pparg
Itga5
Myc
Ednra
Sell
Hgf
Mmp2
Edn1
Syk
Fos
Il1b
-3
-2
-1
0
logFC

FIG. 8B

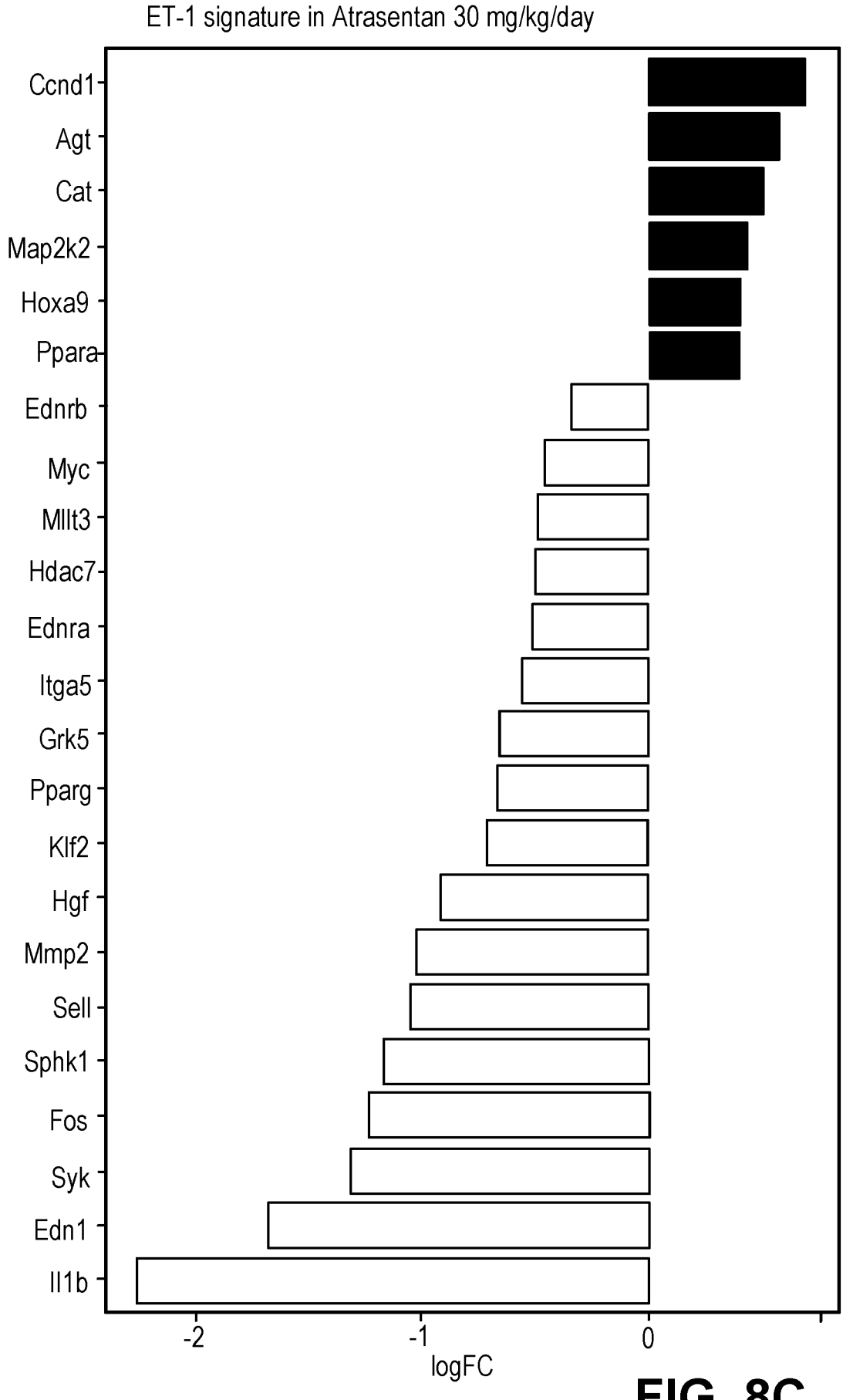

ET-1 signature in Atrasentan 30 mg/kg/day
Ccnd1
Agt
Cat
Map2k2
Hoxa9
Ppara
Ednrb
Myc
Mllt3
Hdac7
Ednra
Itga5
Grk5
Pparg
Klf2
Hgf
Mmp2
Sell
Sphk1
Fos
Syk
Edn1
Il1b
-2
-1
0
logFC

FIG. 8C

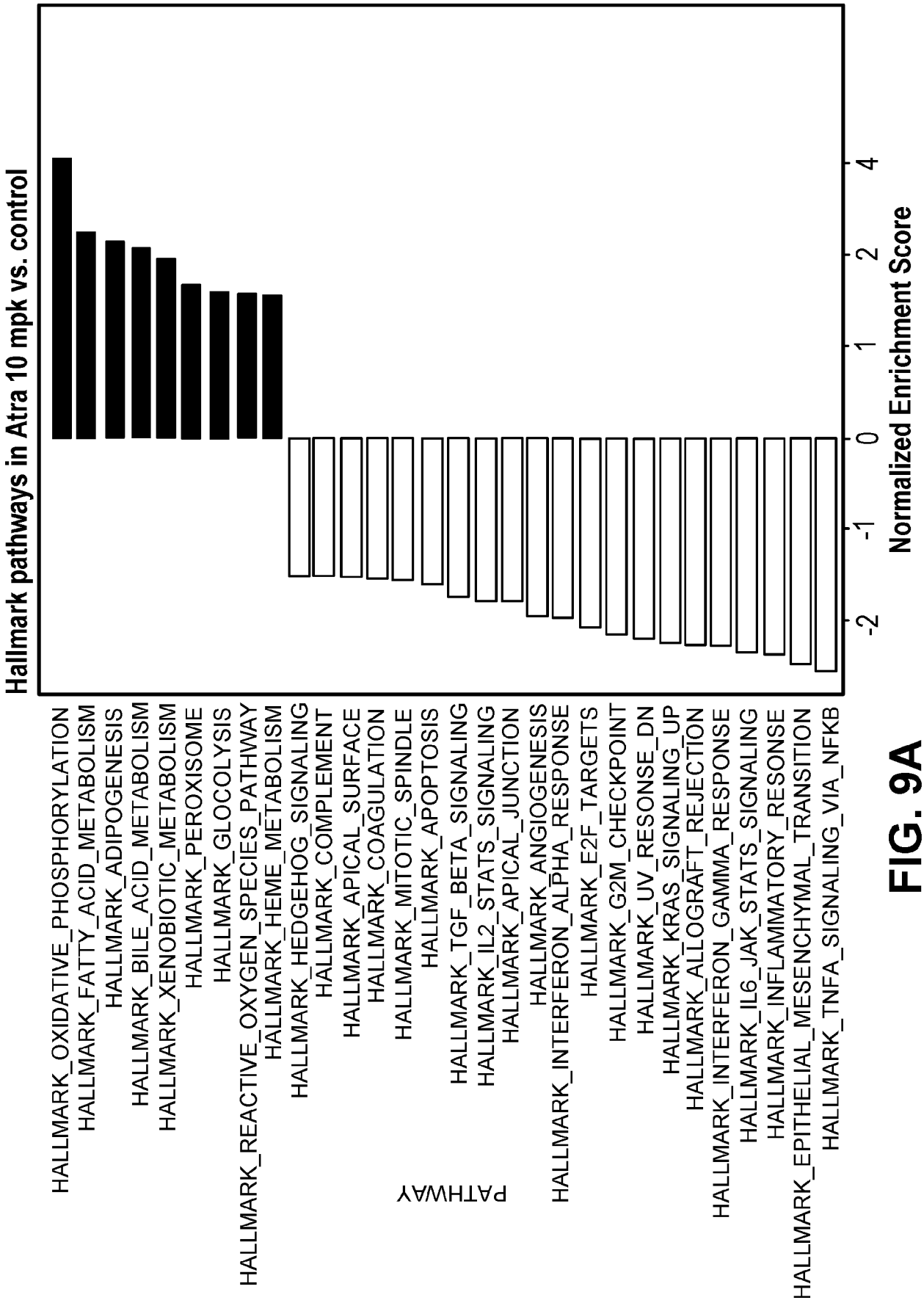

Hallmark pathways in Atra 10 mpk vs. control
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_ADIPOGENESIS
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_PEROXISOME
HALLMARK_GLOCOLYSIS
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_HEME_METABOLISM
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_COMPLEMENT
HALLMARK_APICAL_SURFACE
HALLMARK_COAGULATION
HALLMARK_MITOTIC_SPINDLE
HALLMARK_APOPTOSIS
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_IL2_STATS_SIGNALING
HALLMARK_APICAL_JUNCTION
HALLMARK_ANGIOGENESIS
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_E2F_TARGETS
HALLMARK_G2M_CHECKPOINT
HALLMARK_UV_RESONSE_DN
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_IL6_JAK_STATS_SIGNALING
HALLMARK_INFLAMMATORY_RESONSE
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_TNFA_SIGNALING_VIA_NFKB
PATHWAY
-2
-1
0
1
2
4
Normalized Enrichment Score

FIG. 9A

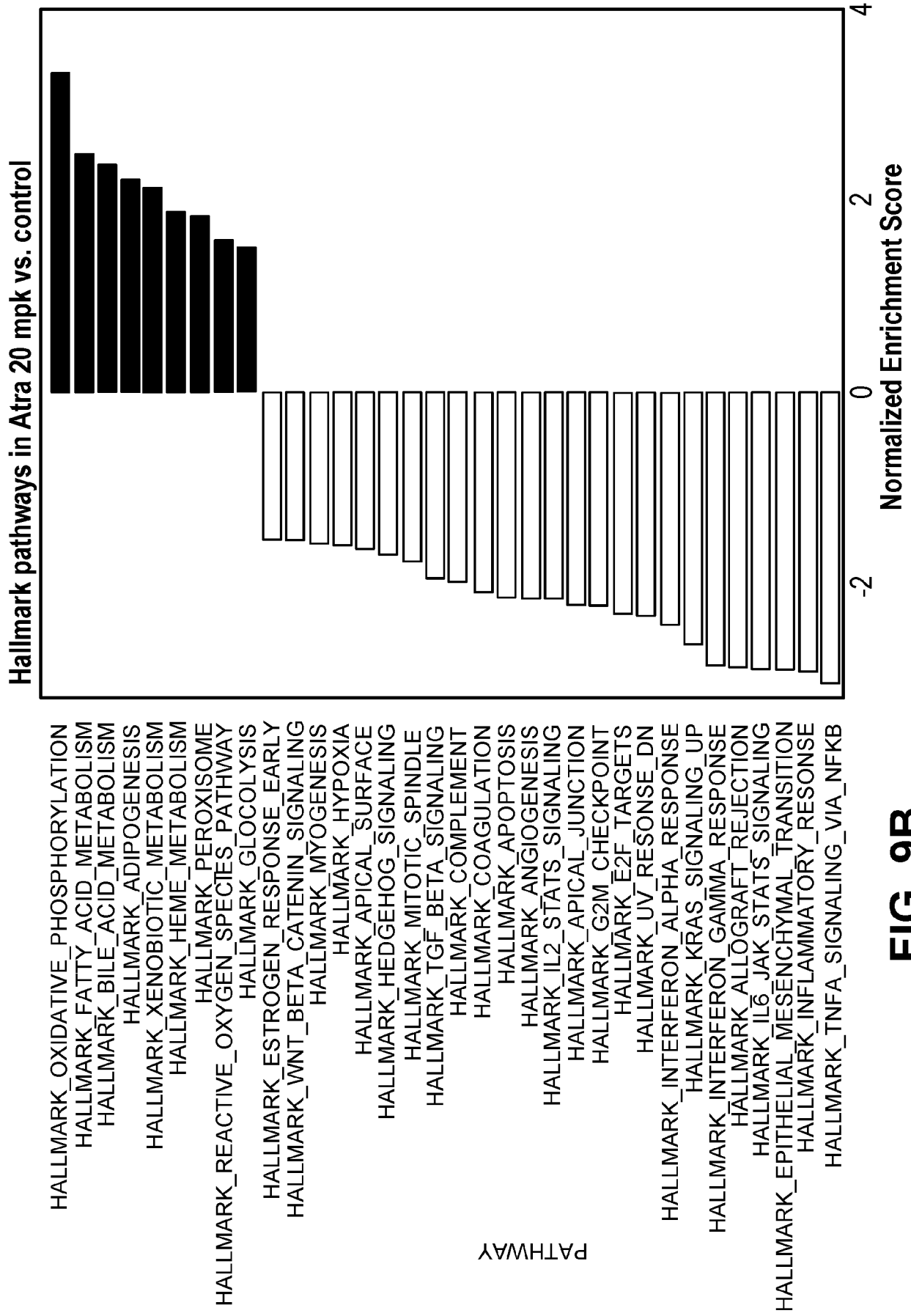

Hallmark pathways in Atra 20 mpk vs. control
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_ADIPOGENESIS
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_HEME_METABOLISM
HALLMARK_PEROXISOME
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_GLYCOLYSIS
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_MYOGENESIS
HALLMARK_HYPOXIA
HALLMARK_APICAL_SURFACE
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_MITOTIC_SPINDLE
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_COMPLEMENT
HALLMARK_COAGULATION
HALLMARK_APOPTOSIS
HALLMARK_ANGIOGENESIS
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_APICAL_JUNCTION
HALLMARK_G2M_CHECKPOINT
HALLMARK_E2F_TARGETS
HALLMARK_UV_RESPONSE_DN
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_INFLAMMATORY_RESONSE
HALLMARK_TNFA_SIGNALING_VIA_NFKB
PATHWAY
-2
0
2
4
Normalized Enrichment Score

FIG. 9B

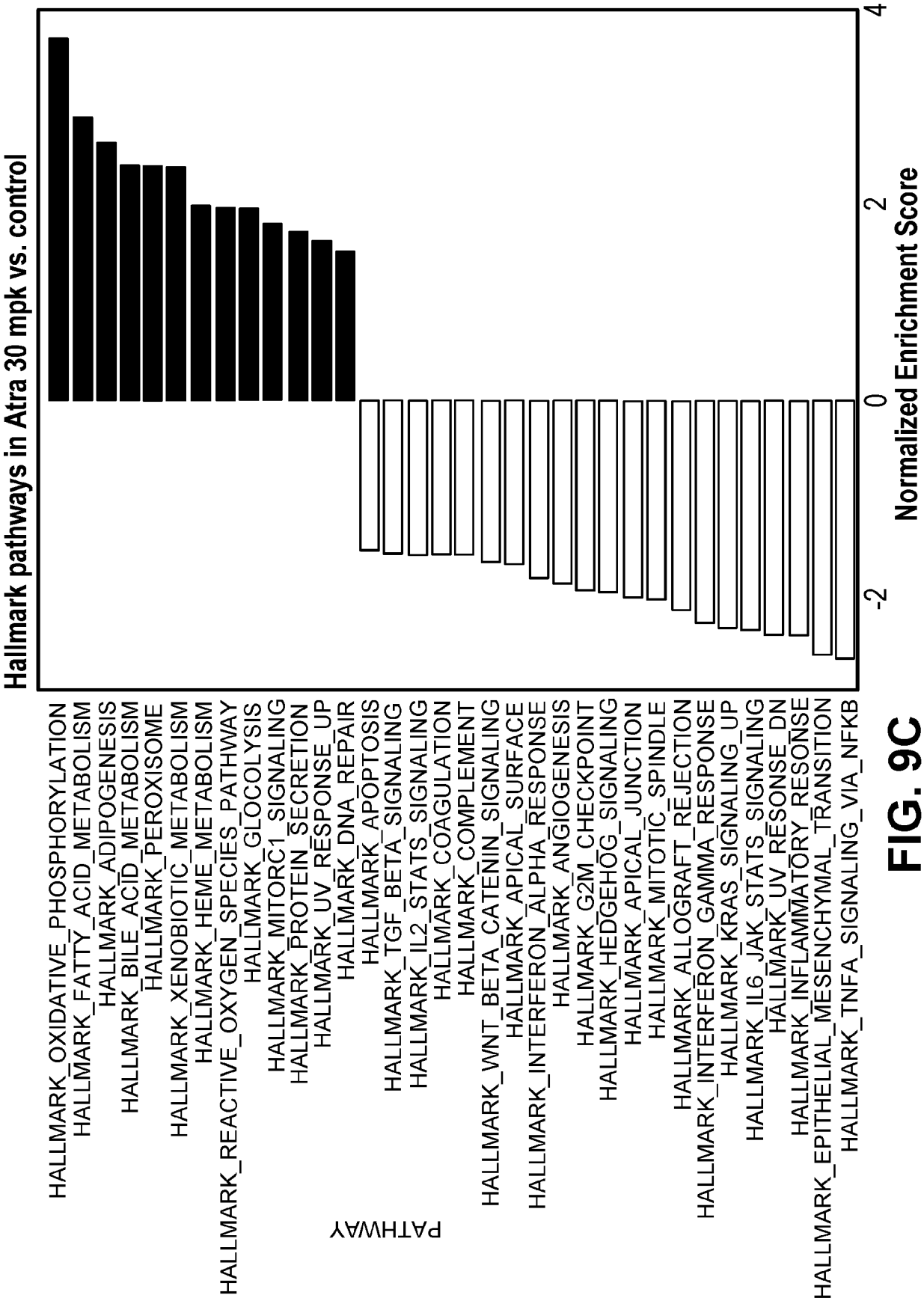

Hallmark pathways in Atra 30 mpk vs. control
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_ADIPOGENESIS
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_PEROXISOME
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_HEME_METABOLISM
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_GLYCOLYSIS
HALLMARK_MITORC1_SIGNALING
HALLMARK_PROTEIN_SECRETION
HALLMARK_UV_RESPONSE_UP
HALLMARK_DNA_REPAIR
HALLMARK_APOPTOSIS
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_COAGULATION
HALLMARK_COMPLEMENT
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_APICAL_SURFACE
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_ANGIOGENESIS
HALLMARK_G2M_CHECKPOINT
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_APICAL_JUNCTION
HALLMARK_MITOTIC_SPINDLE
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_UV_RESPONSE_DN
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_TNFA_SIGNALING_VIA_NFKB
PATHWAY
-2
0
2
4
Normalized Enrichment Score

FIG. 9C

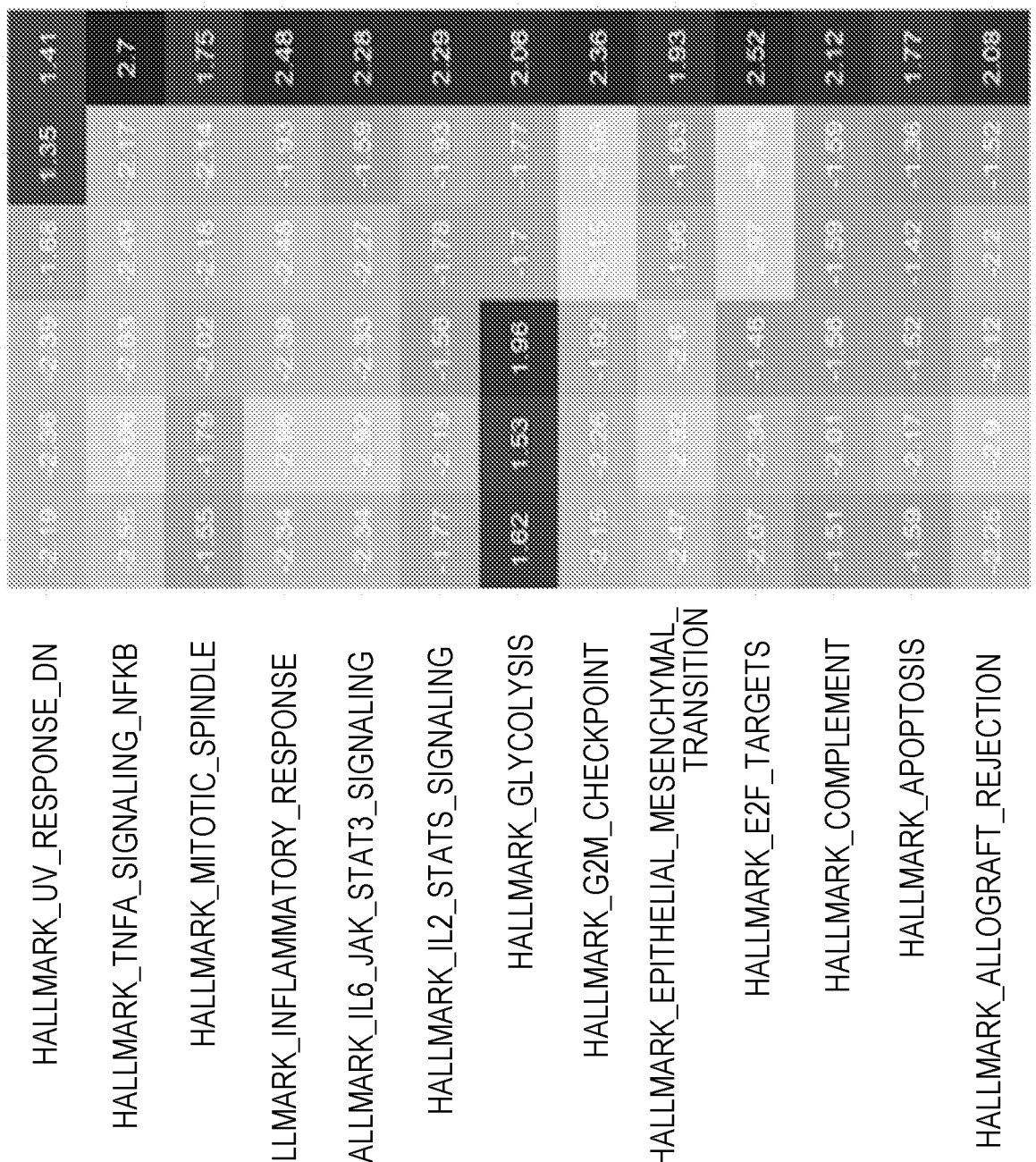

NES_score
2
1
0
-1
-2
-3
HALLMARK_UV_RESPONSE_DN
HALLMARK_TNFA_SIGNALING_NFKB
HALLMARK_MITOTIC_SPINDLE
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_GLYCOLYSIS
HALLMARK_G2M_CHECKPOINT
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_E2F_TARGETS
HALLMARK_COMPLEMENT
HALLMARK_APOPTOSIS
HALLMARK_ALLOGRAFT_REJECTION
gddy.10mg
gddy.20mg
gddy.30mg
HRMC.1nM
HRMC.25nM
HRMC.ET1

FIG. 10

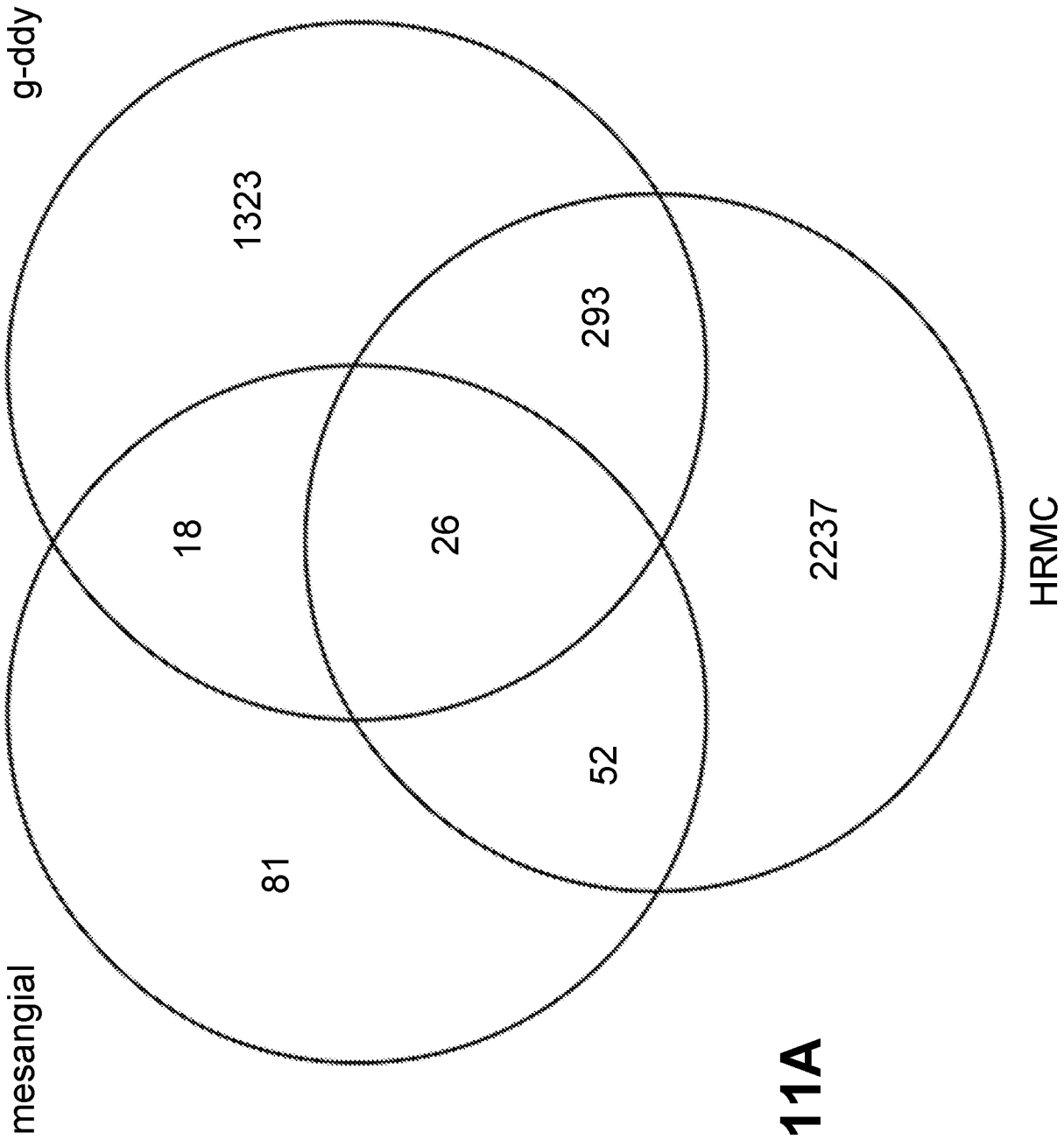


FIG. 11A

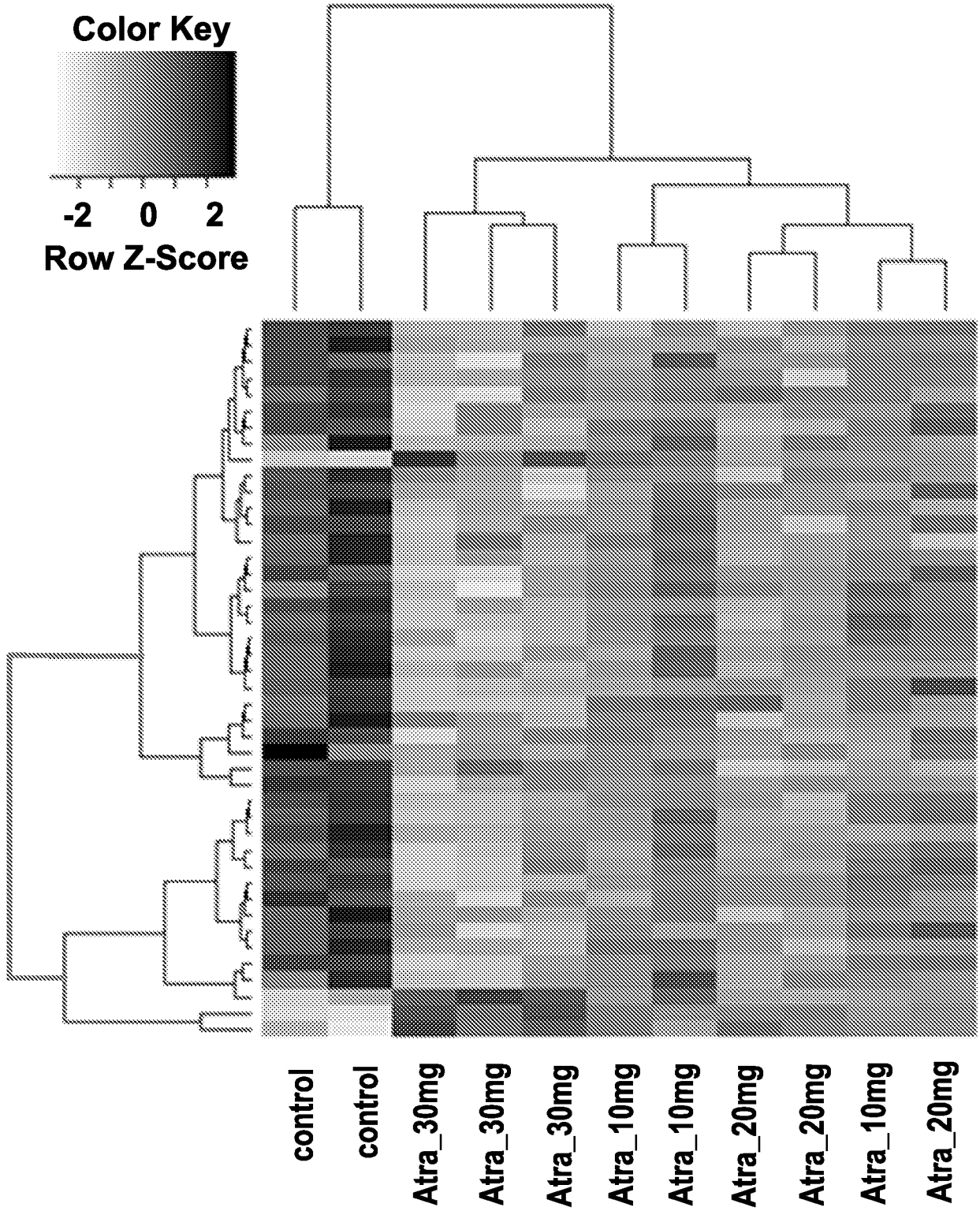

Color Key
-2
0
2
Row Z-Score
control
control
Atra_30mg
Atra_30mg
Atra_30mg
Atra_10mg
Atra_10mg
Atra_20mg
Atra_20mg
Atra_10mg
Atra_20mg

FIG. 11B

/ Symbol Entrez Gene Name		Human	Mouse	Plasma/Serum	Urine
ALPL	alkaline phosphatase, biomineralization associated	X	X	X	X
AMIN	amnion associated transmembrane protein	X	X		X
ASL	argininosuccinate lyase	X	X	X	
CRYL1	crystallin lamda 1	X	X		X
DPEP1	dipeptidase 1	X	X		X
GAPDH	glyceraldehyde-3-phosphate dehydrogenase	X	X	X	X
IGF1	insulin like growth factor 1	X	X	X	X
PDZK1IP1	PDZK1 interacting protein 1	X	X		X
PEBP1	phosphatidylethanolamine binding protein 1	X	X		X
SELENBP1	selenium binding protein 1	X	X	X	X
SLC19A1	solute carrier family 19 member 1	X	X	X	
SLC6A19	solute carrier family 6 member 19	X	X		X

FIG. 12A

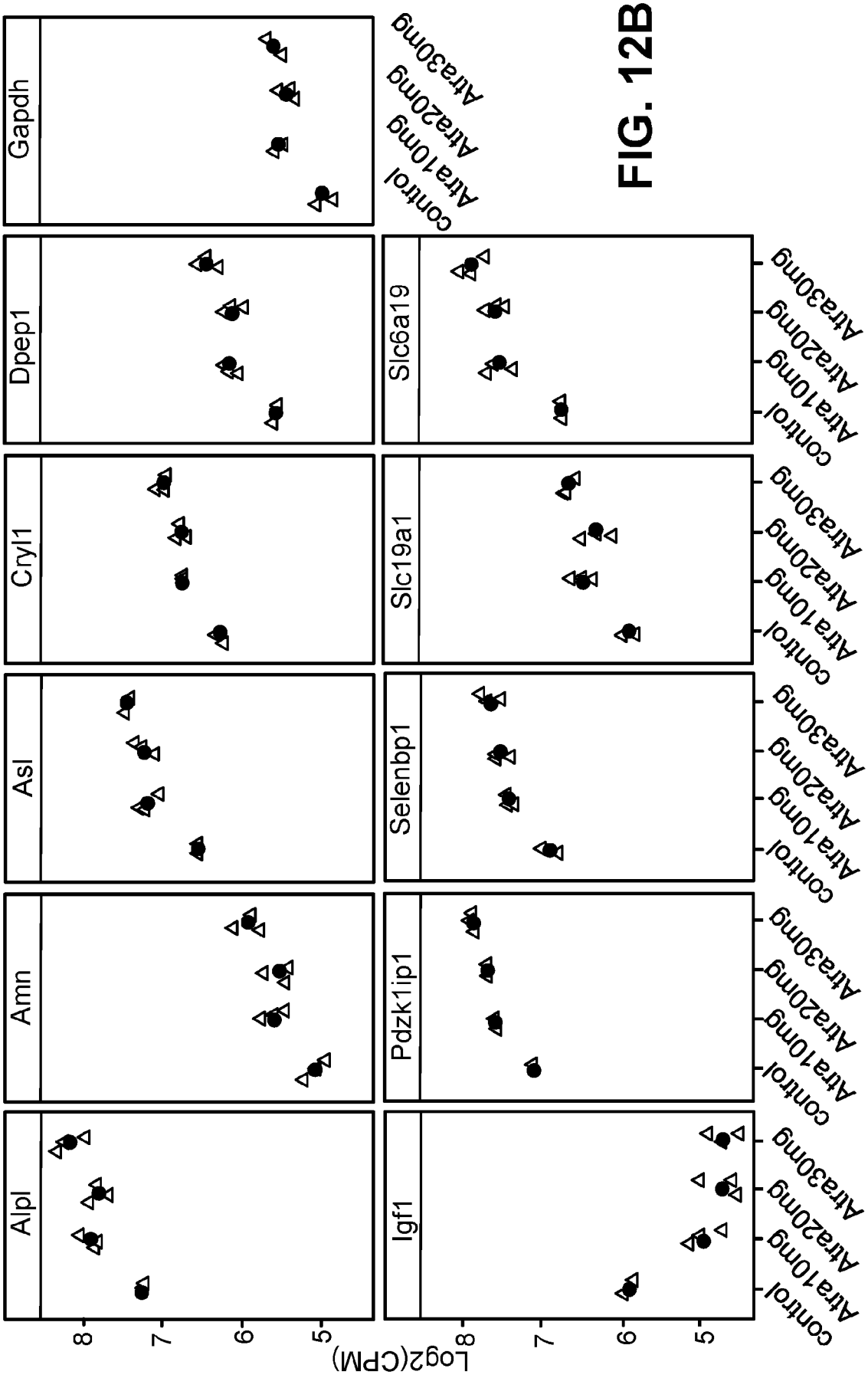

Alpl
Amn
Asl
Cryl1
Dpep1
Gapdh
Igf1
Pdzk1ip1
Selenbp1
Slc19a1
Slc6a19
Log2(CPM)
8
7
6
5
control
Ata10mg
Ata20mg
Ata30mg

FIG. 12B