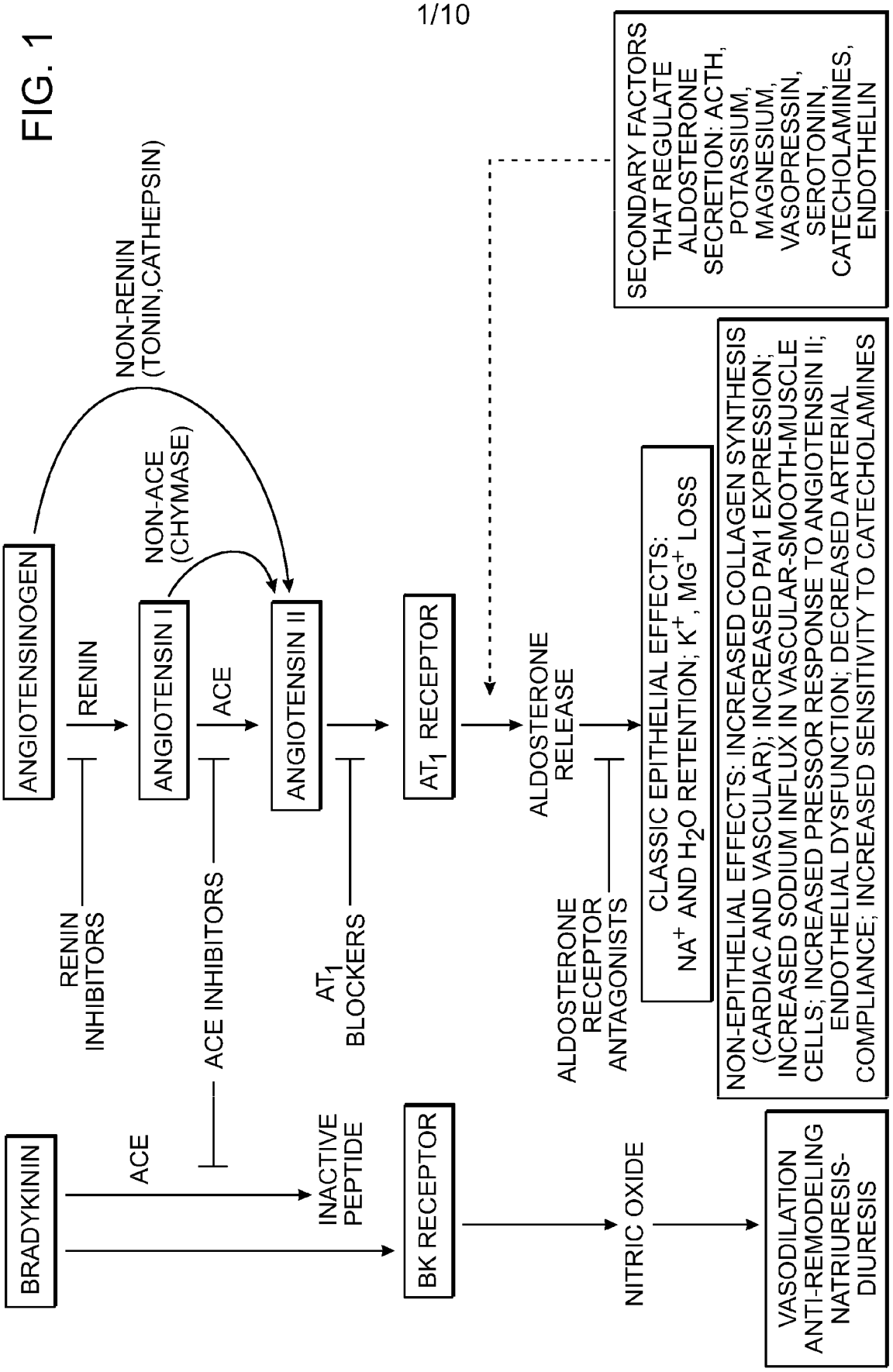
FIG. 1


ANGIOTENSINOGEN
RENIN
ANGIOTENSIN I
NON-RENIN
(TONIN,CATHEPSIN)
NON-ACE
(CHYMASE)
ACE
ANGIOTENSIN II
AT1 RECEPTOR
ALDOSTERONE
RELEASE
SECONDARY FACTORS
THAT REGULATE
ALDOSTERONE
SECRETION: ACTH,
POTASSIUM,
MAGNESIUM,
VASOPRESSIN,
SERETONIN,
CATECHOLAMINES,
ENDOTHELIN
RENIN
INHIBITORS
ACE INHIBITORS
AT1
BLOCKERS
ALDOSTERONE
RECEPTOR
ANTAGONISTS
CLASSIC EPITHELIAL EFFECTS:
NA+ AND H2O RETENTION; K+, MG+ LOSS
NON-EPITHELIAL EFFECTS: INCREASED COLLAGEN SYNTHESIS
(CARDIAC AND VASCULAR); INCREASED PAI1 EXPRESSION;
INCREASED SODIUM INFLUX IN VASCULAR-SMOOTH-MUSCLE
CELLS; INCREASED PRESSOR RESPONSE TO ANGIOTENSIN II;
ENDOTHELIAL DYSFUNCTION; DECREASED ARTERIAL
COMPLIANCE; INCREASED SENSITIVITY TO CATECHOLAMINES
BRADYKININ
ACE
INACTIVE
PEPTIDE
BK RECEPTOR
NITRIC OXIDE
VASODILATION
ANTI-REMODELING
NATRIURESIS-
DIURESIS

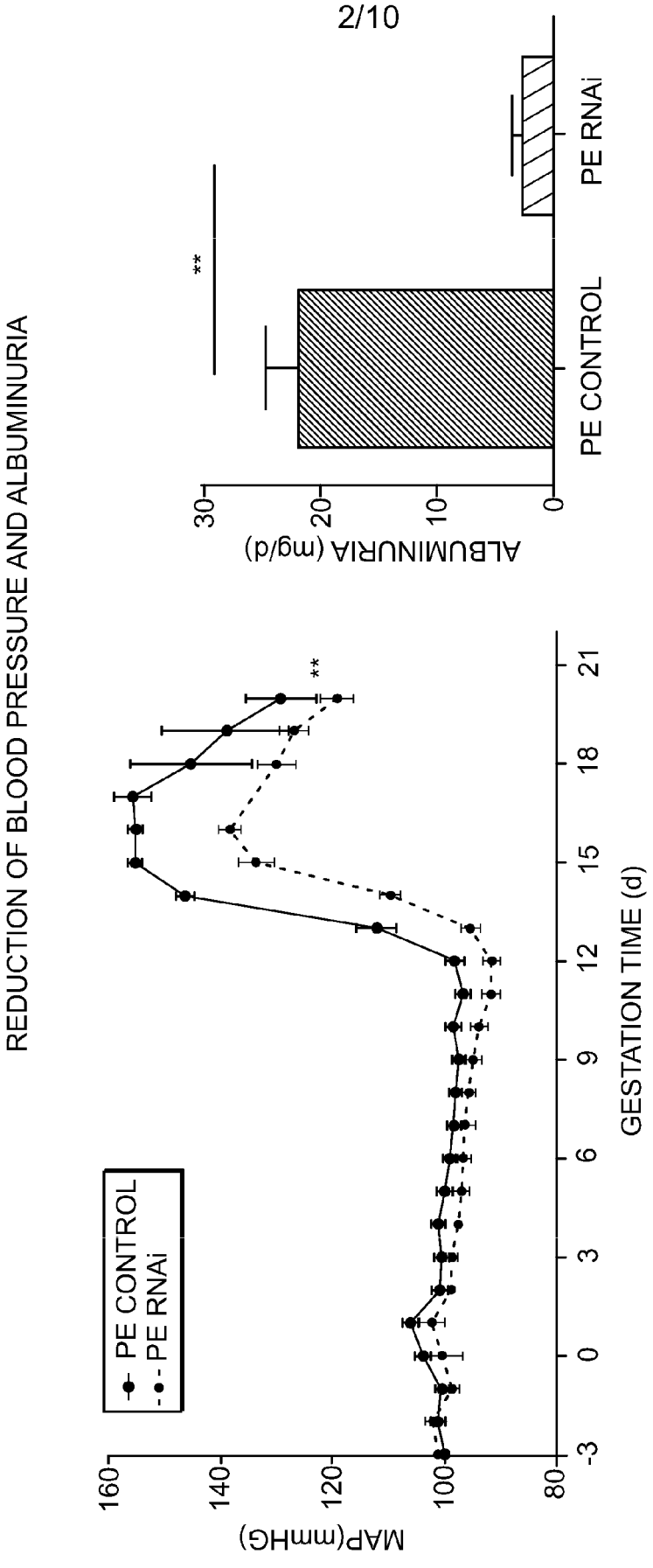

REDUCTION OF BLOOD PRESSURE AND ALBUMINURIA
MAP(mmHG)
160
140
120
100
80
-3
0
3
6
9
12
15
18
21
GESTATION TIME (d)
PE CONTROL
PE RNAi
**
ALBUMINURIA (mg/d)
30
20
10
0
**
PE CONTROL
PE RNAi

FIG. 2A

FIG. 2B

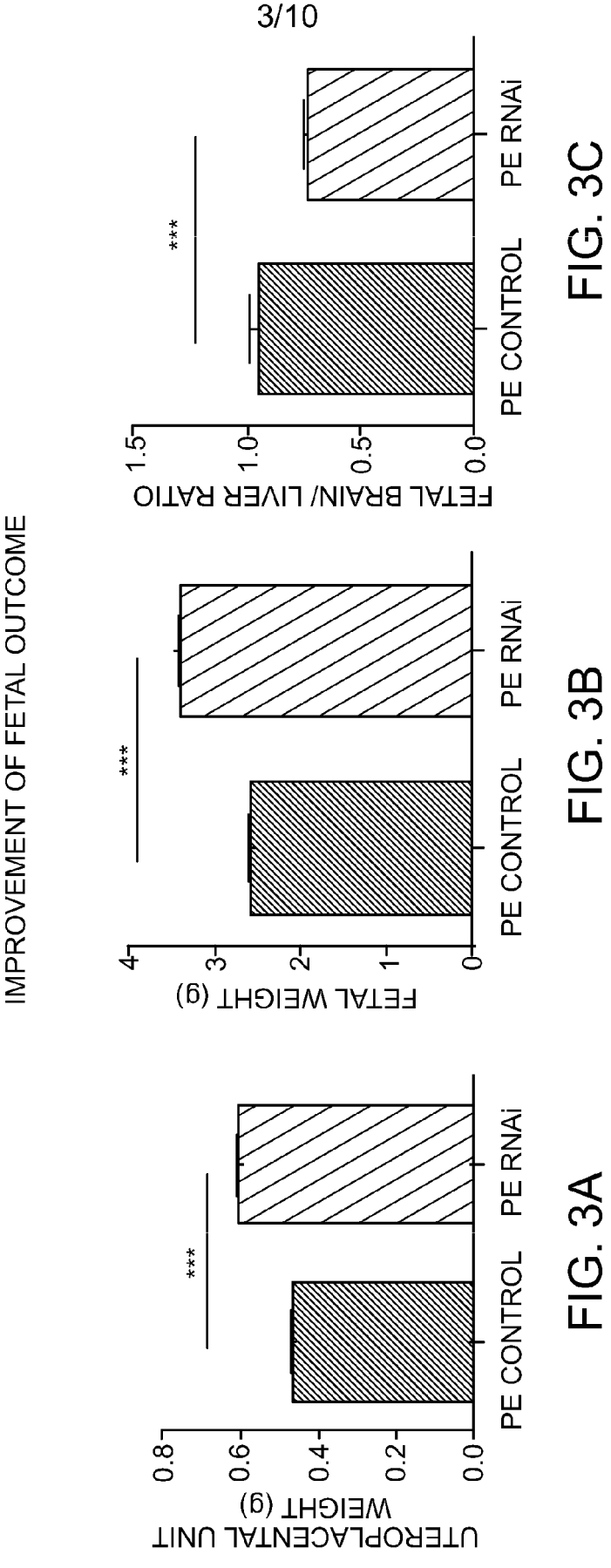


FIG. 3A

FIG. 3B

FIG. 3C

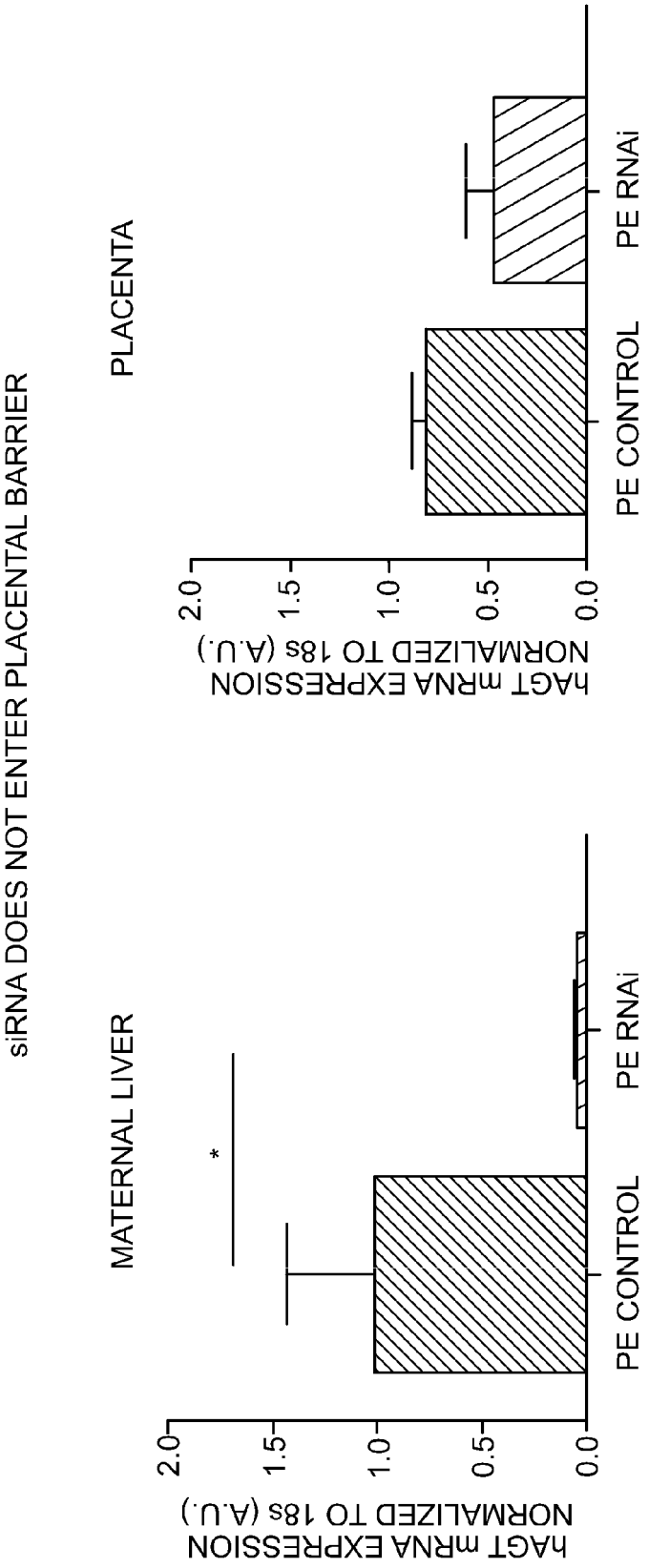

siRNA DOES NOT ENTER PLACENTAL BARRIER
MATERNAL LIVER
hAGT mRNA EXPRESSION
NORMALIZED TO 18s (A.U.)
2.0
1.5
1.0
0.5
0.0
*
PE CONTROL
PE RNAi
PLACENTA
hAGT mRNA EXPRESSION
NORMALIZED TO 18s (A.U.)
2.0
1.5
1.0
0.5
0.0
PE CONTROL
PE RNAi

FIG. 4A

FIG. 4B

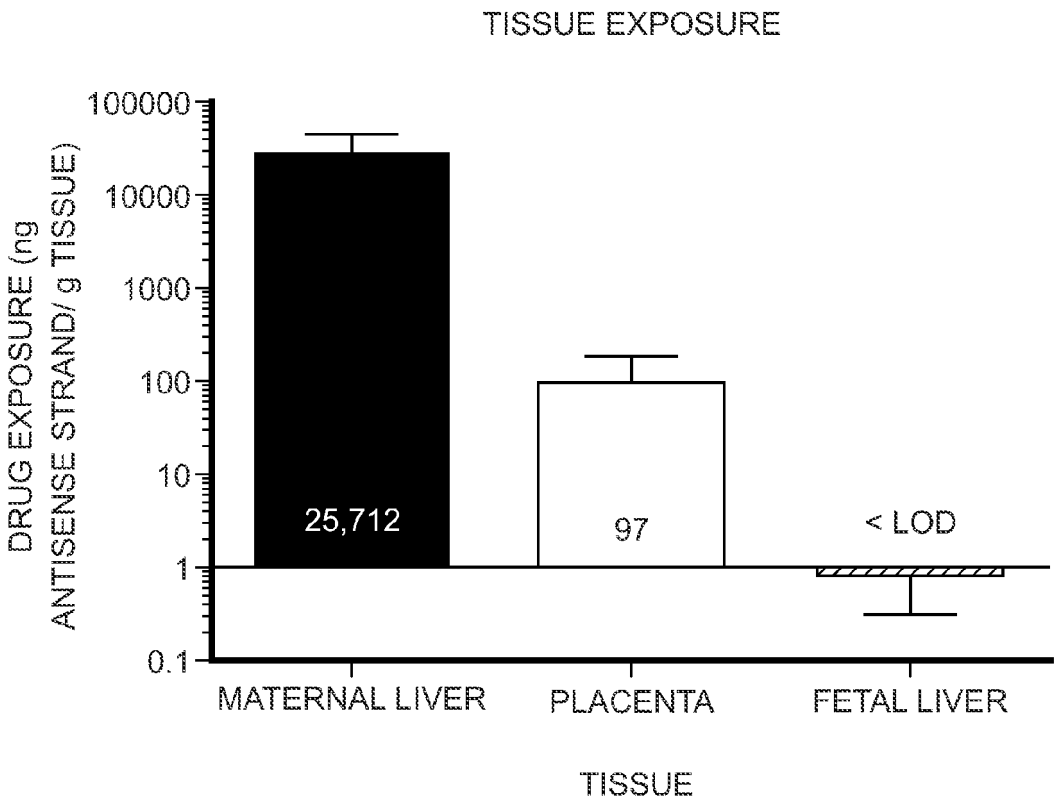

TISSUE EXPOSURE
DRUG EXPOSURE (ng ANTISENSE STRAND/ g TISSUE)
100000
10000
1000
100
10
1
0.1
25,712
97
< LOD
MATERNAL LIVER
PLACENTA
FETAL LIVER
TISSUE

FIG. 5

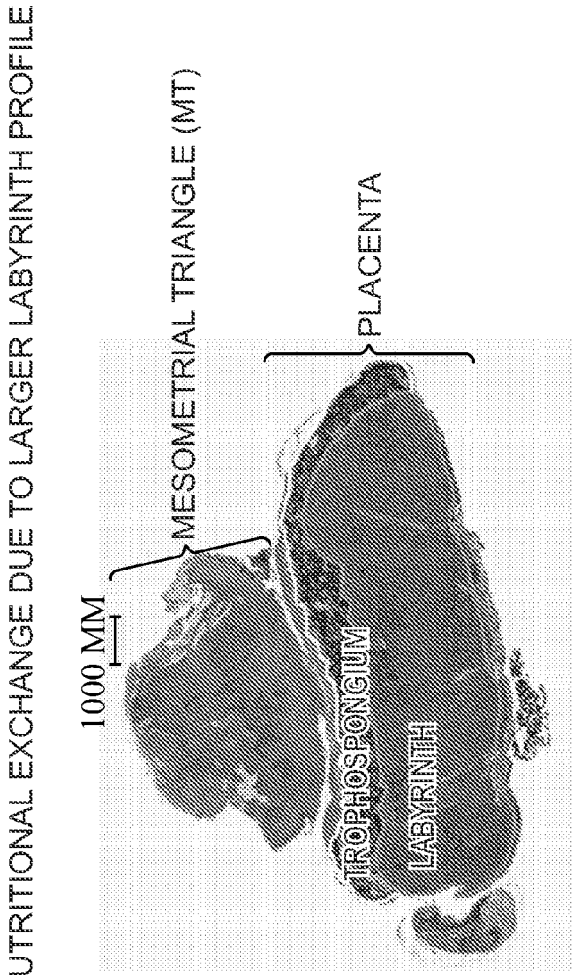


FIG. 6A

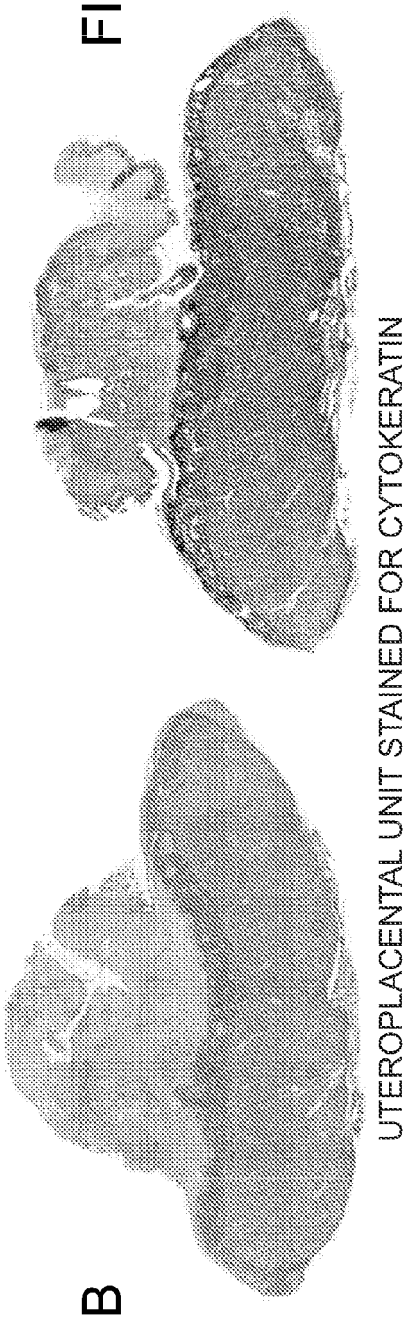


FIG. 6B

FIG. 6C

FIG. 6D

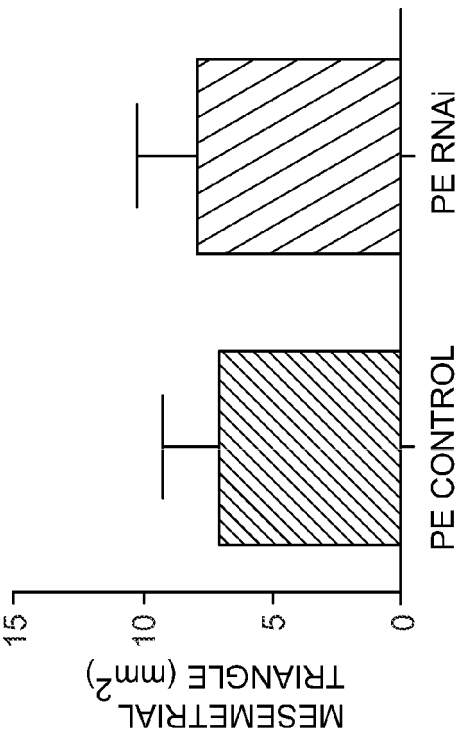


FIG. 6E

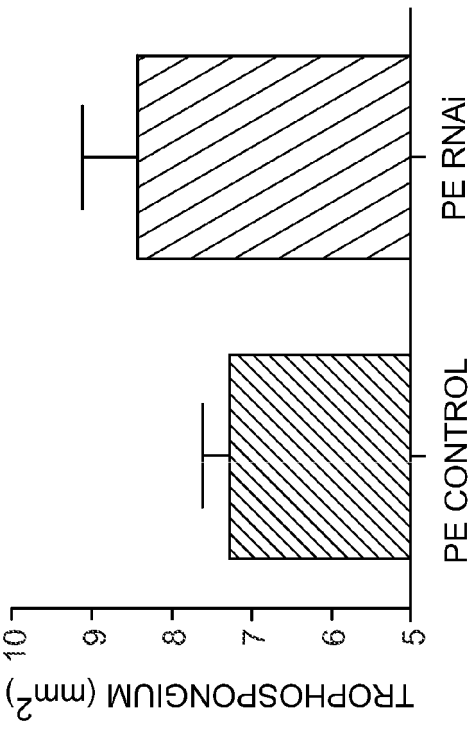


FIG. 6F

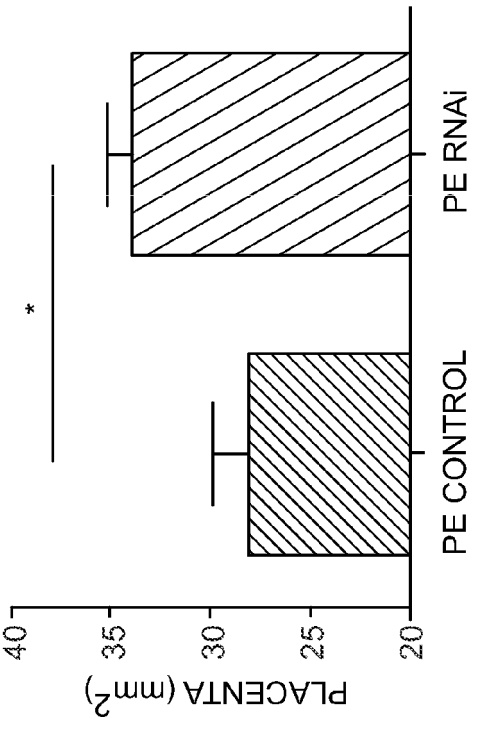
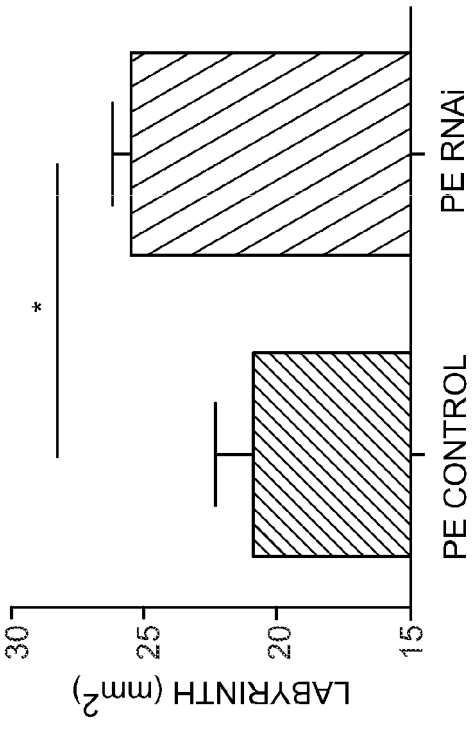


FIG. 6G



REDUCED sFLT1 AND PLGF EXPRESSION IN MATERNAL KIDNEY

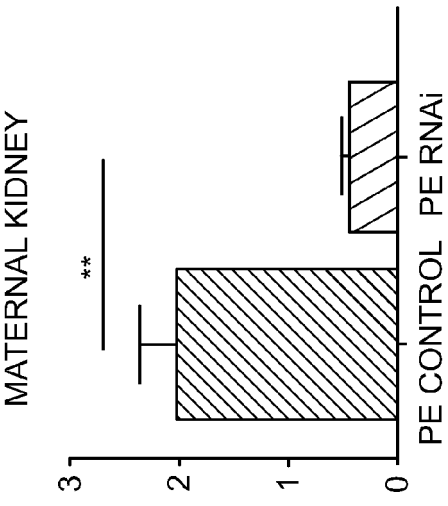


FIG. 7A

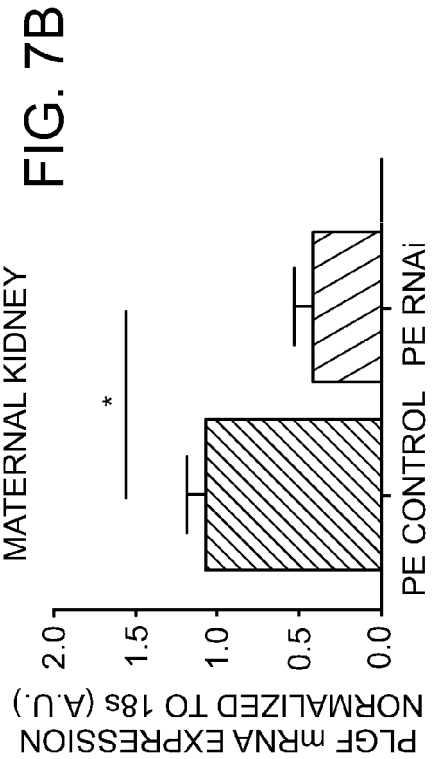


FIG. 7B

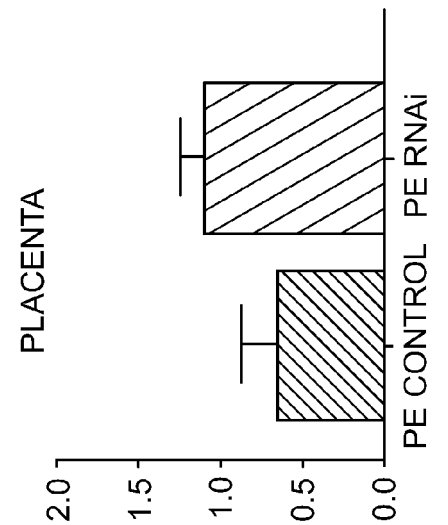


FIG. 7C

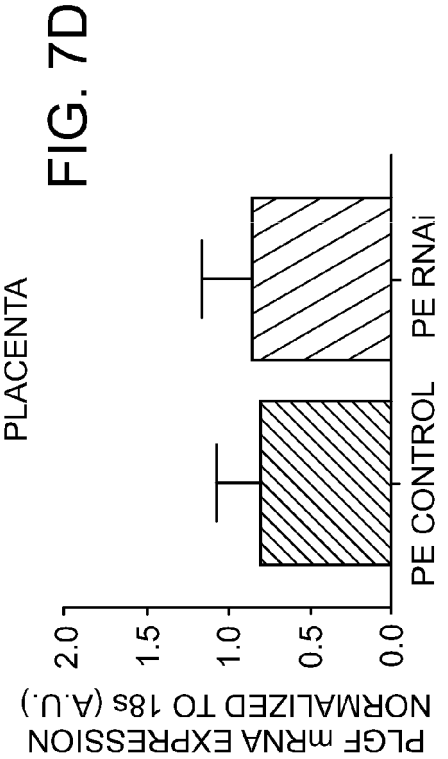


FIG. 7D

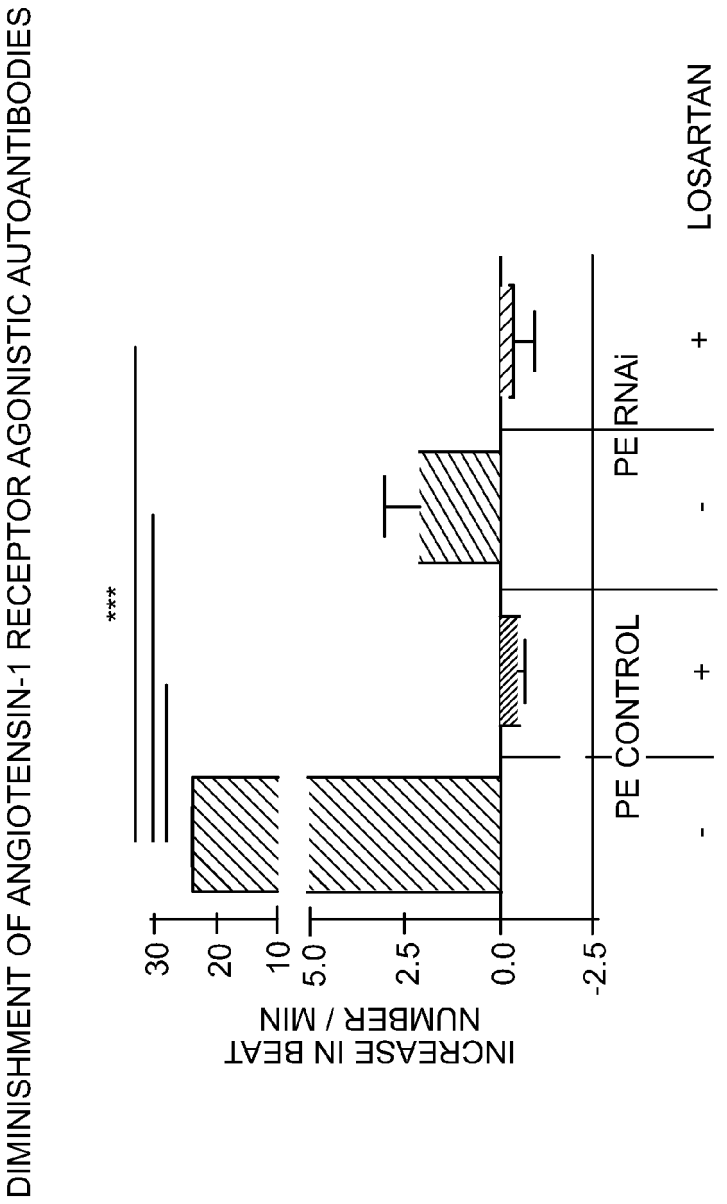

DIMINISHMENT OF ANGIOTENSIN-1 RECEPTOR AGONISTIC AUTOANTIBODIES
INCREASE IN BEAT NUMBER / MIN
30
20
10
5.0
2.5
0.0
-2.5
***
PE CONTROL
PE RNAi
LOSARTAN
-
+
-
+

FIG. 8

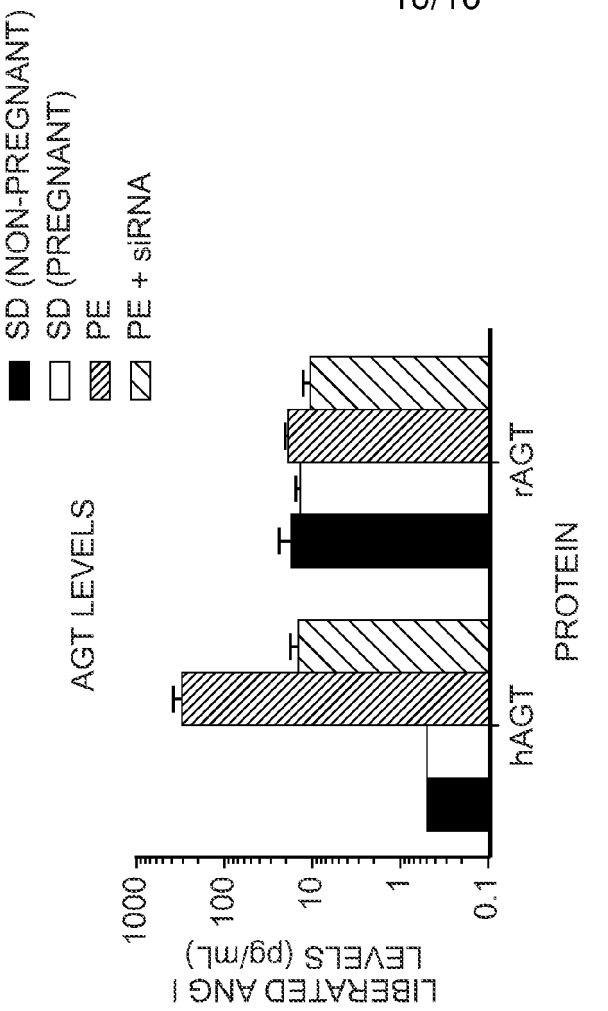

SD (NON-PREGNANT)
SD (PREGNANT)
PE
PE + siRNA
AGT LEVELS
hAGT
rAGT
PROTEIN
1000
100
10
1
0.1
LIBERATED ANG I LEVELS (pg/mL)

FIG. 9B

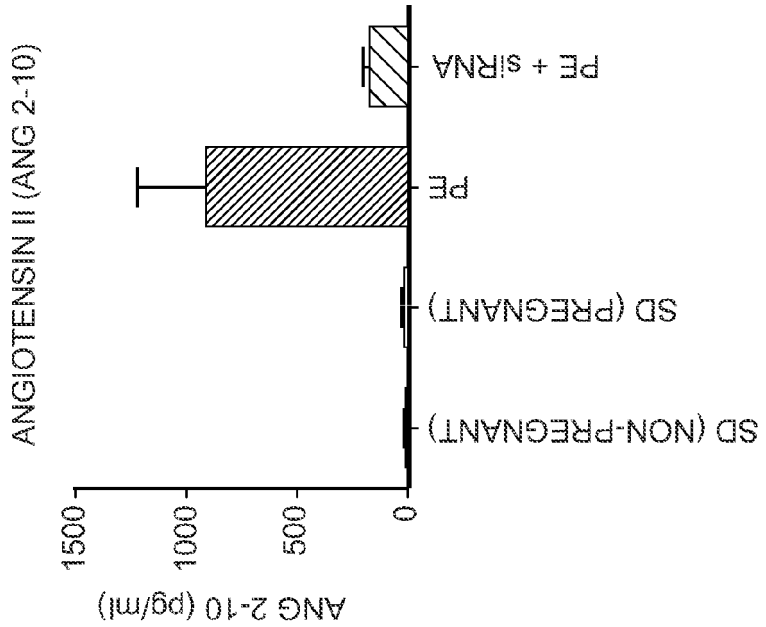

ANGIOTENSIN II (ANG 2-10)
1500
1000
500
0
ANG 2-10 (pg/ml)
SD (NON-PREGNANT)
SD (PREGNANT)
PE
PE + siRNA

FIG. 9A