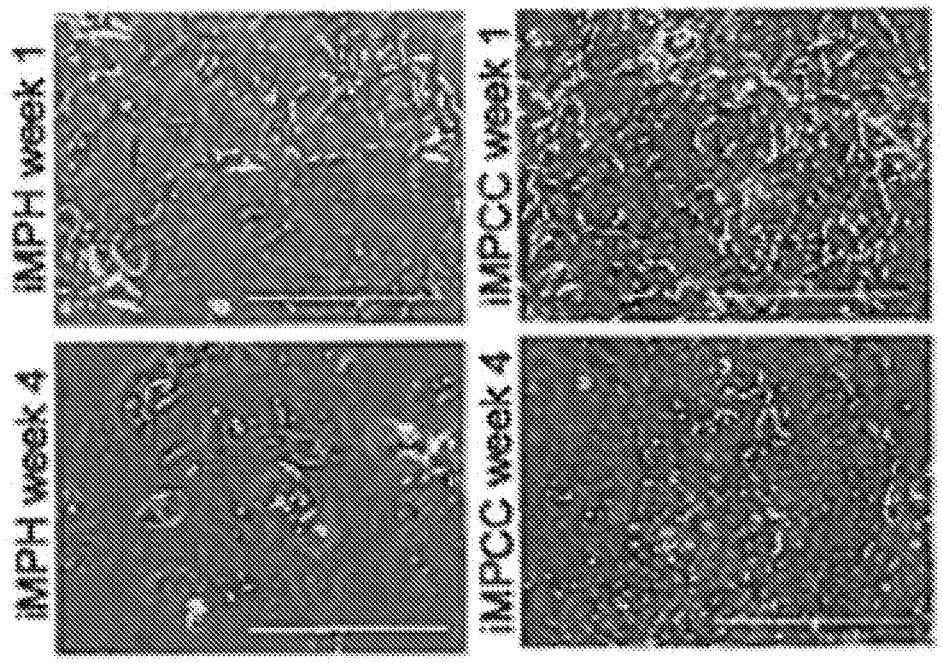
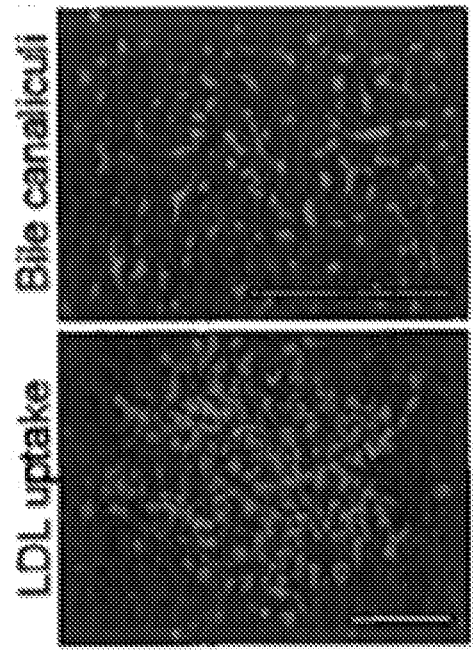
1A



1B



1C

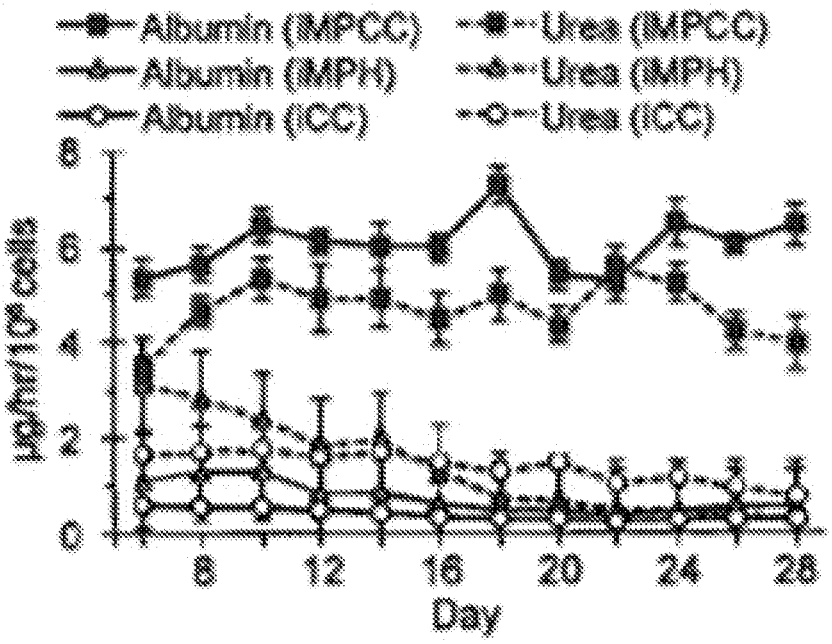
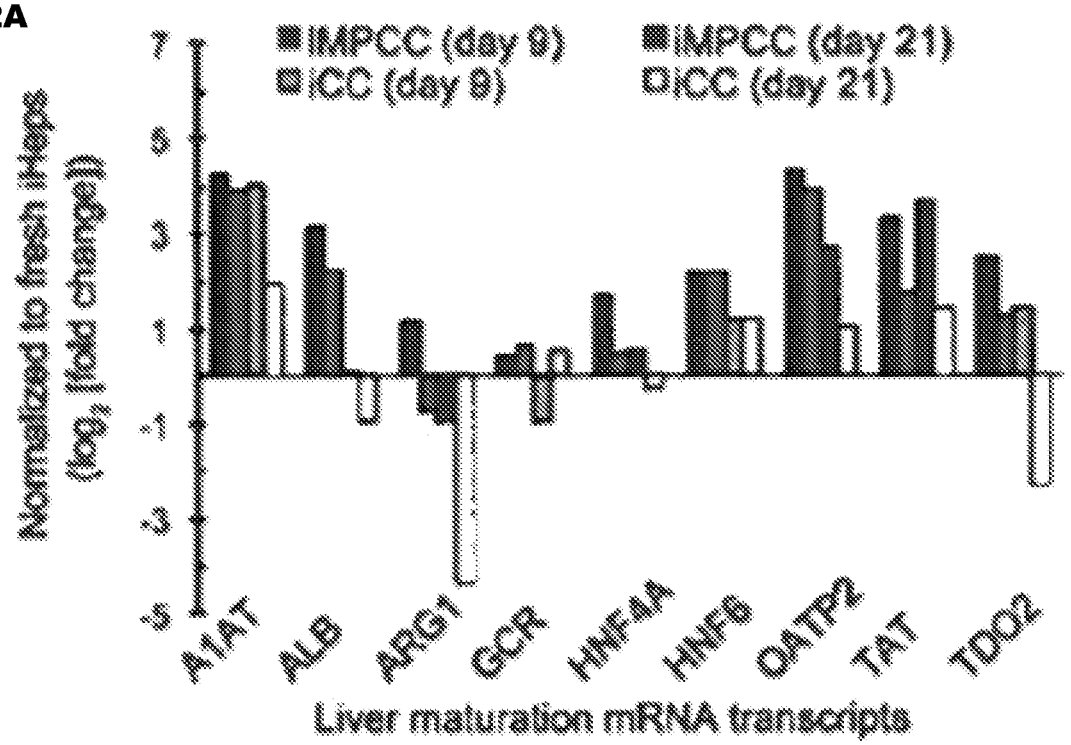


FIGURE 1A, 1B, 1C

2A



2B

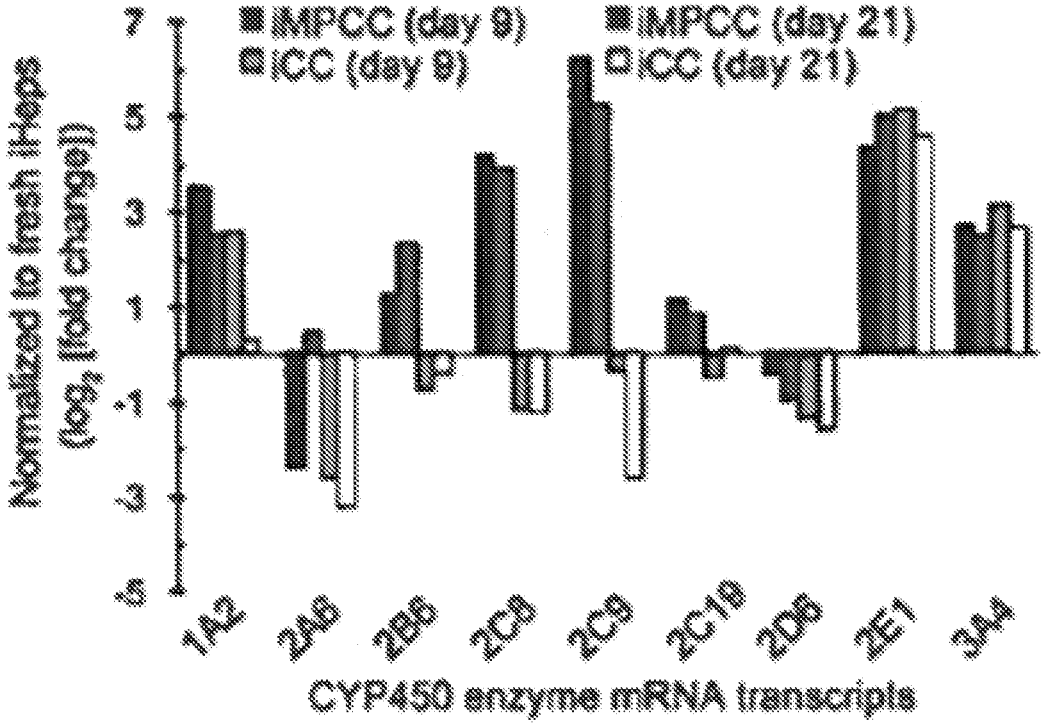
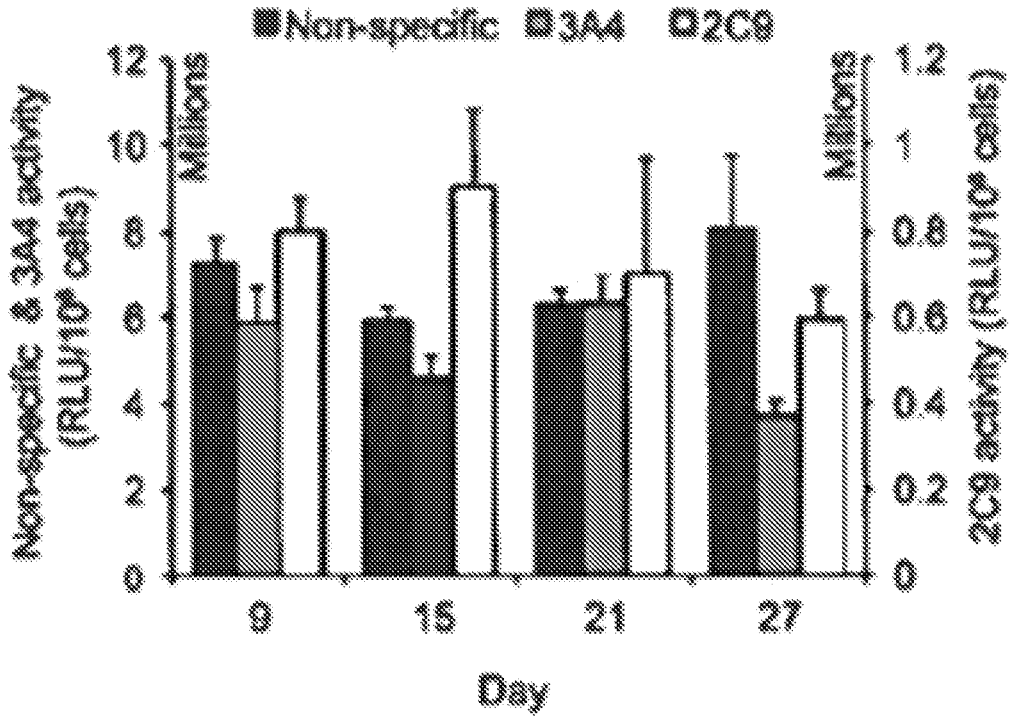
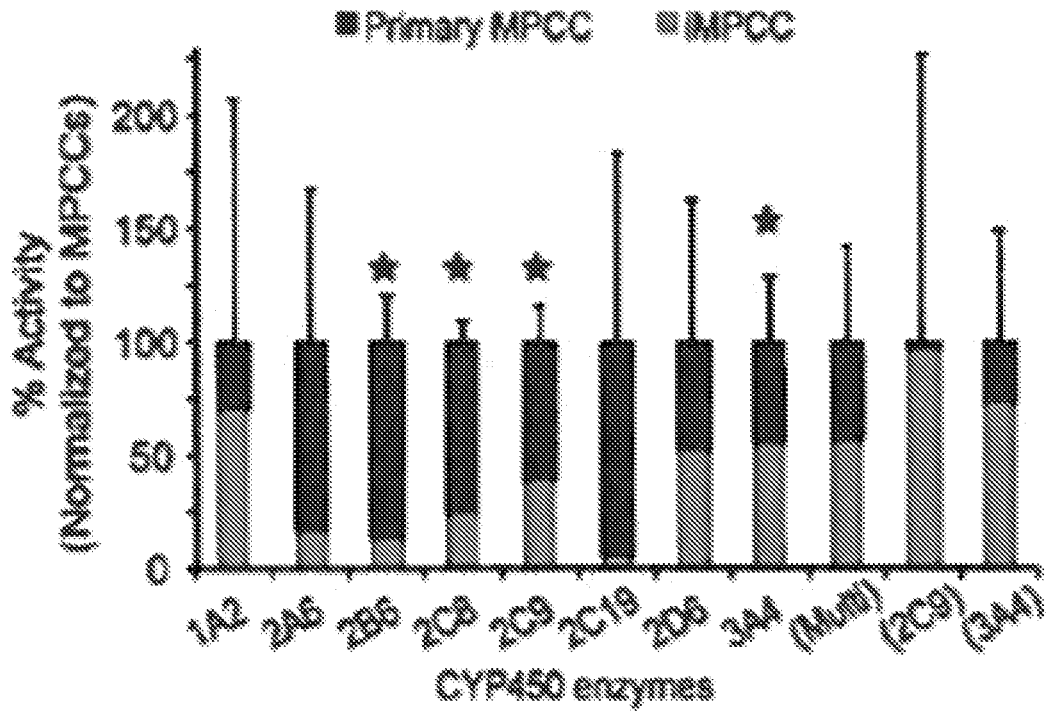


FIGURE 2A, 2B Continued

2C



2D



Continued
FIGURE 2C, 2D

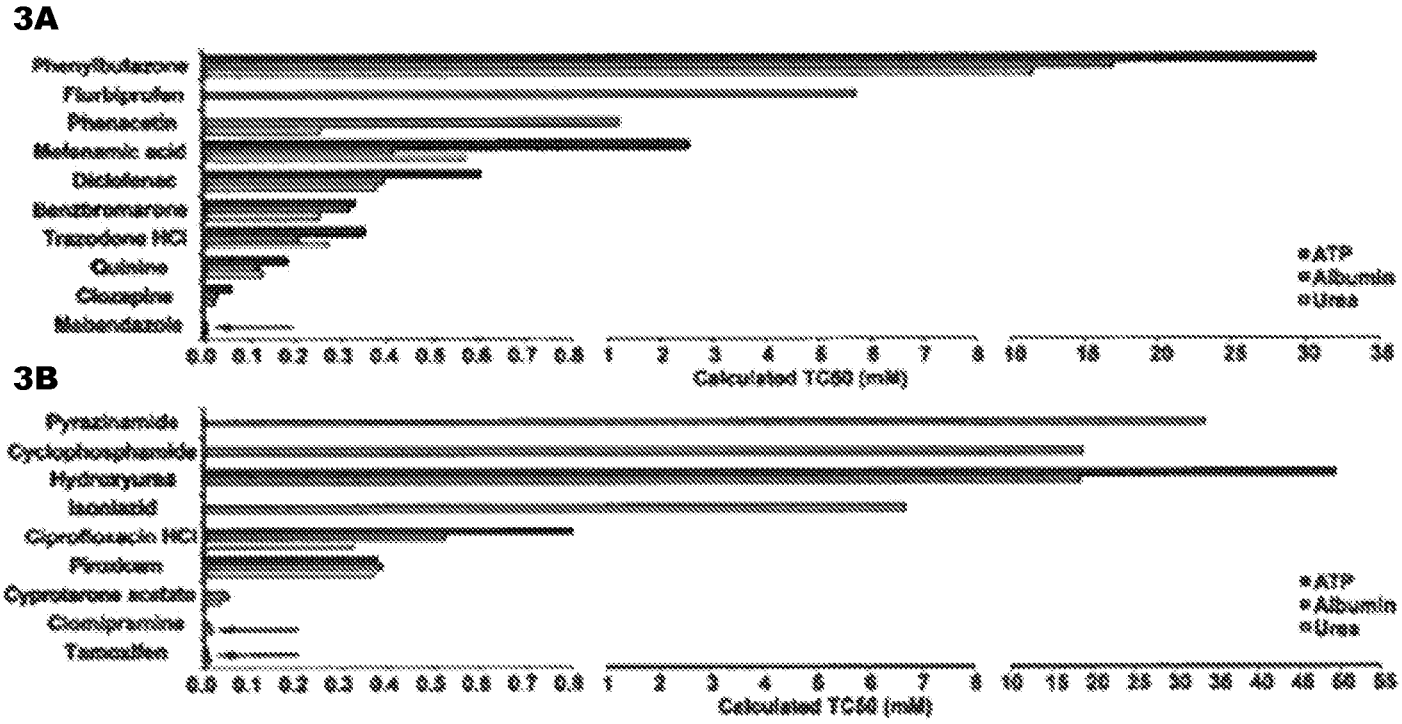
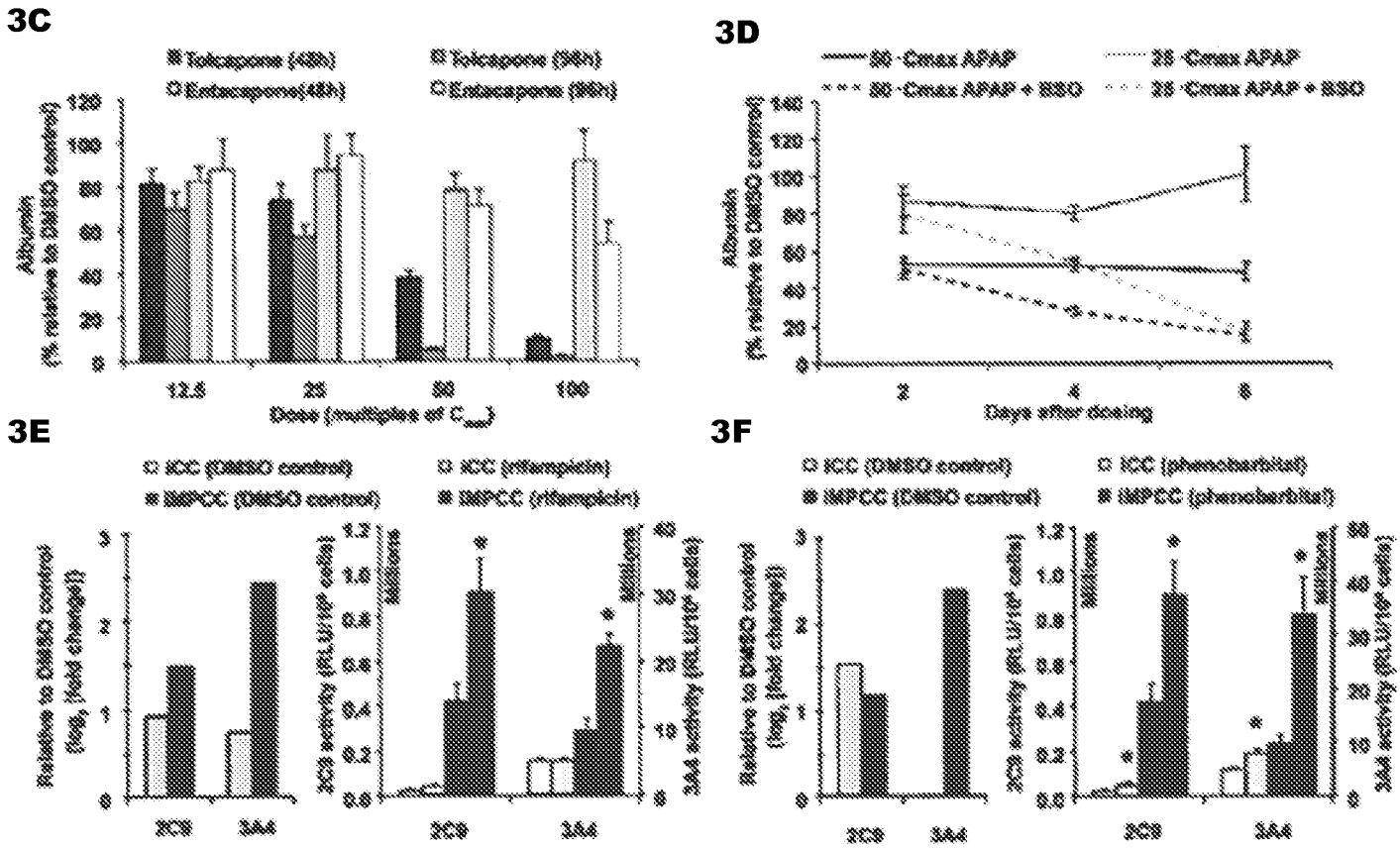


FIGURE 3A, 3B Continued



Continued
FIGURE 3C, 3D, 3E, and 3F

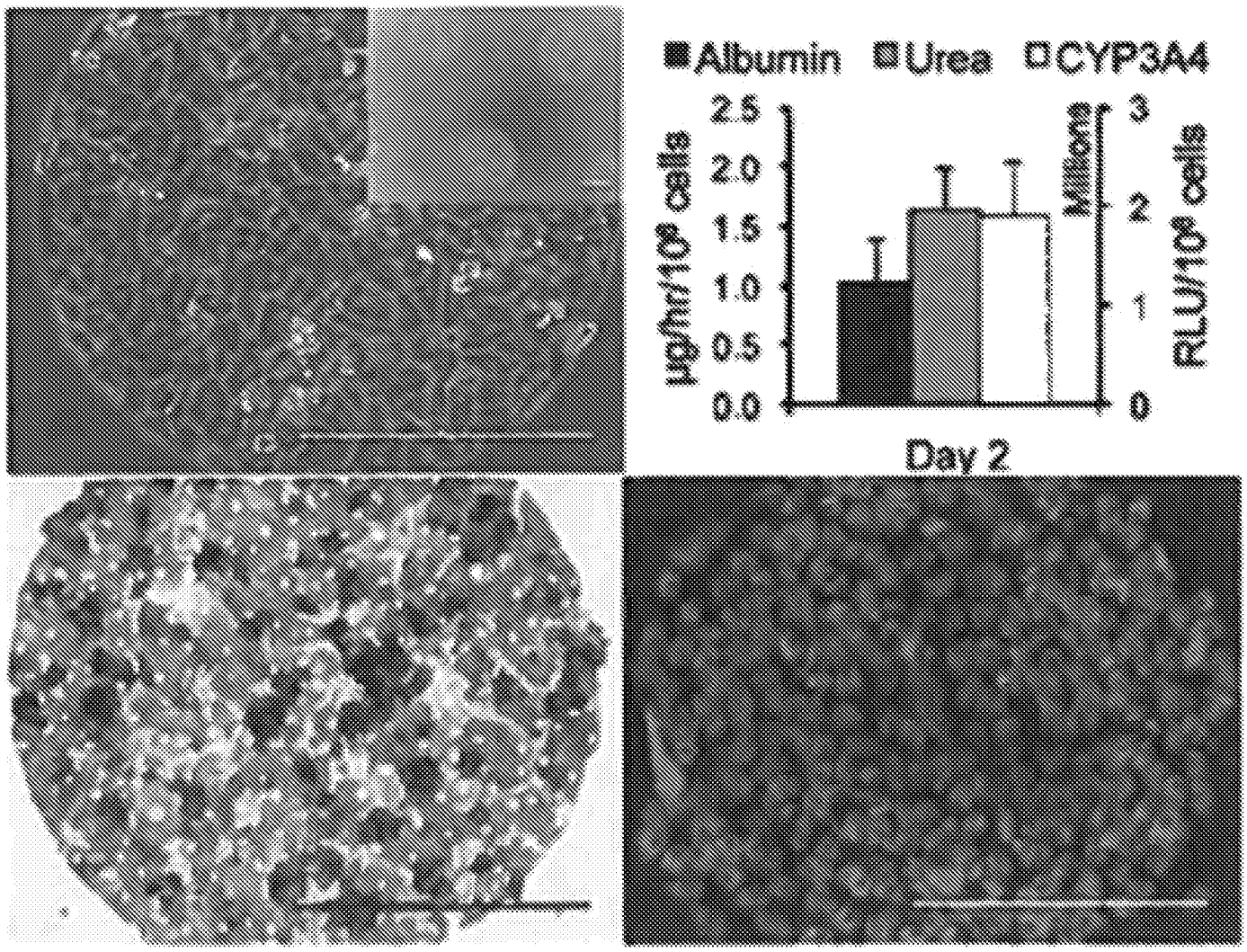

Albumin
Urea
CYP3A4
2.5
2.0
1.5
1.0
0.5
0.0
µg/hr/10⁶ cells
Millions
3
2
1
0
RLU/10⁶ cells
Day 2

FIGURE 4

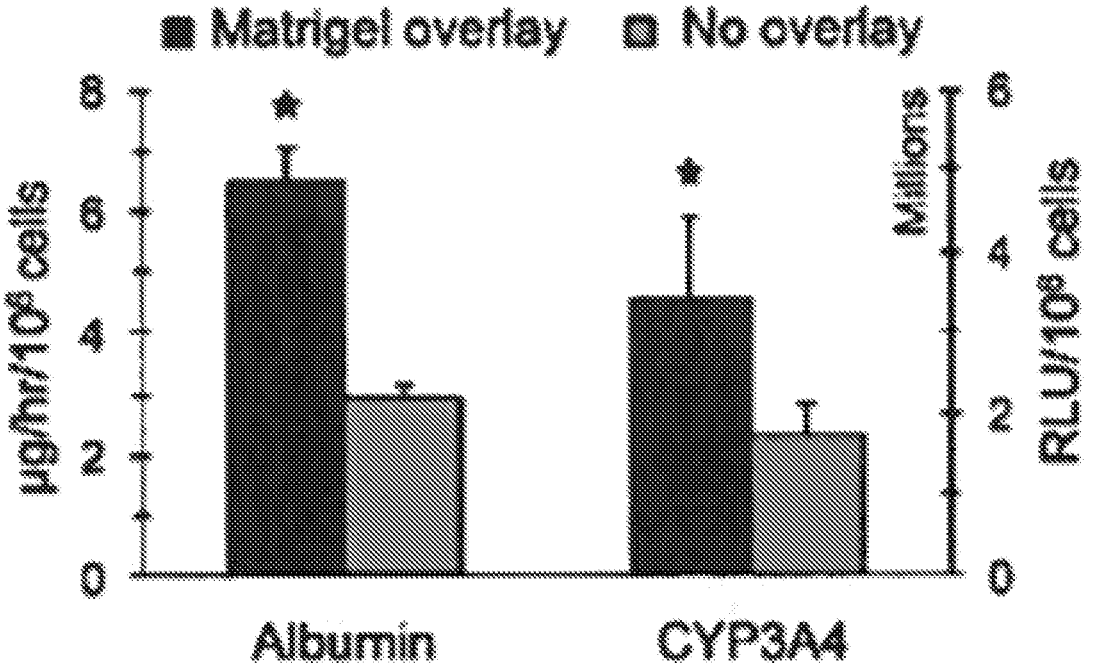
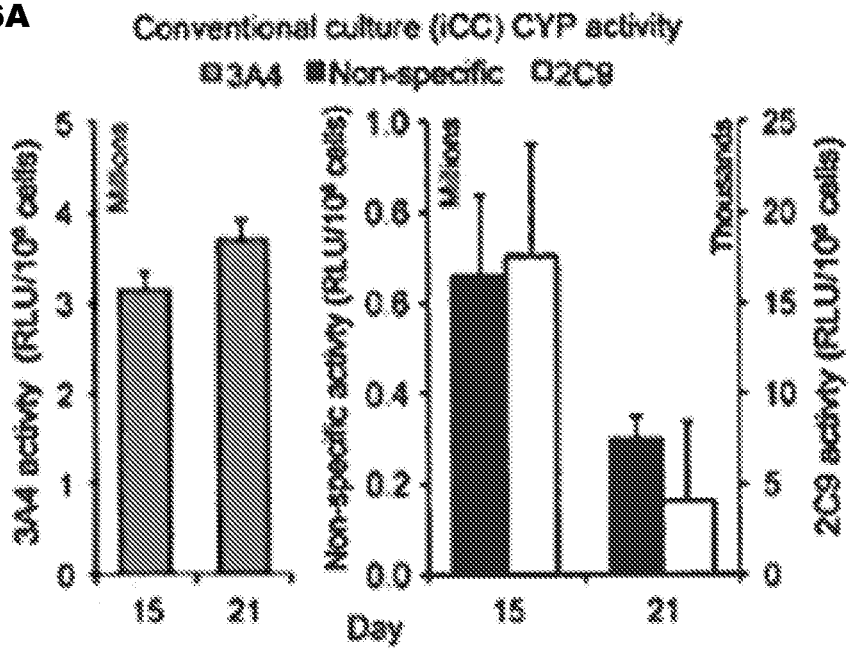

Matrigel overlay
No overlay
µg/hr/10⁶ cells
0
2
4
6
8
Millions
RLU/10⁶ cells
0
2
4
6
Albumin
CYP3A4

FIGURE 5

6A



6B

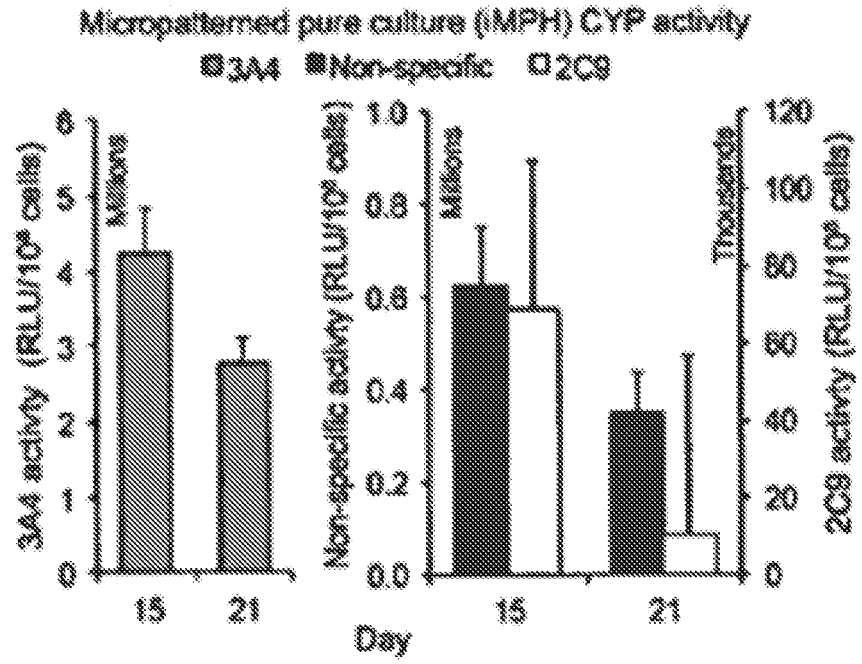


FIGURE 6A and 6B

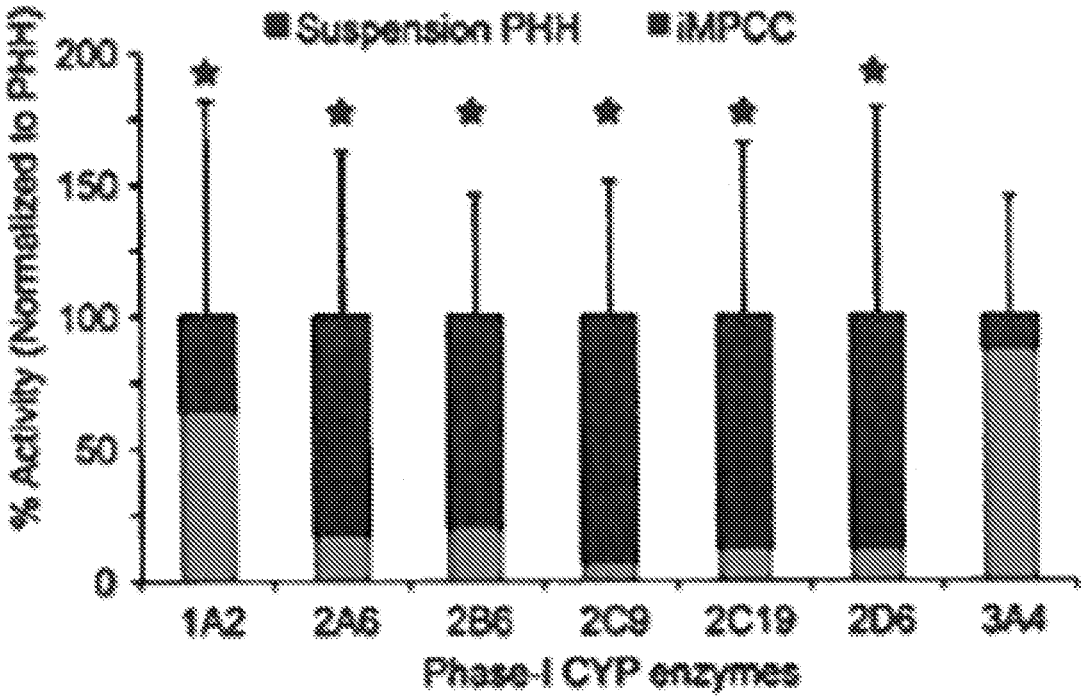

Suspension PHH
iMPCC
% Activity (Normalized to PHH)
200
150
100
50
0
1A2
2A6
2B6
2C9
2C19
2D6
3A4
Phase-I CYP enzymes

FIGURE 7

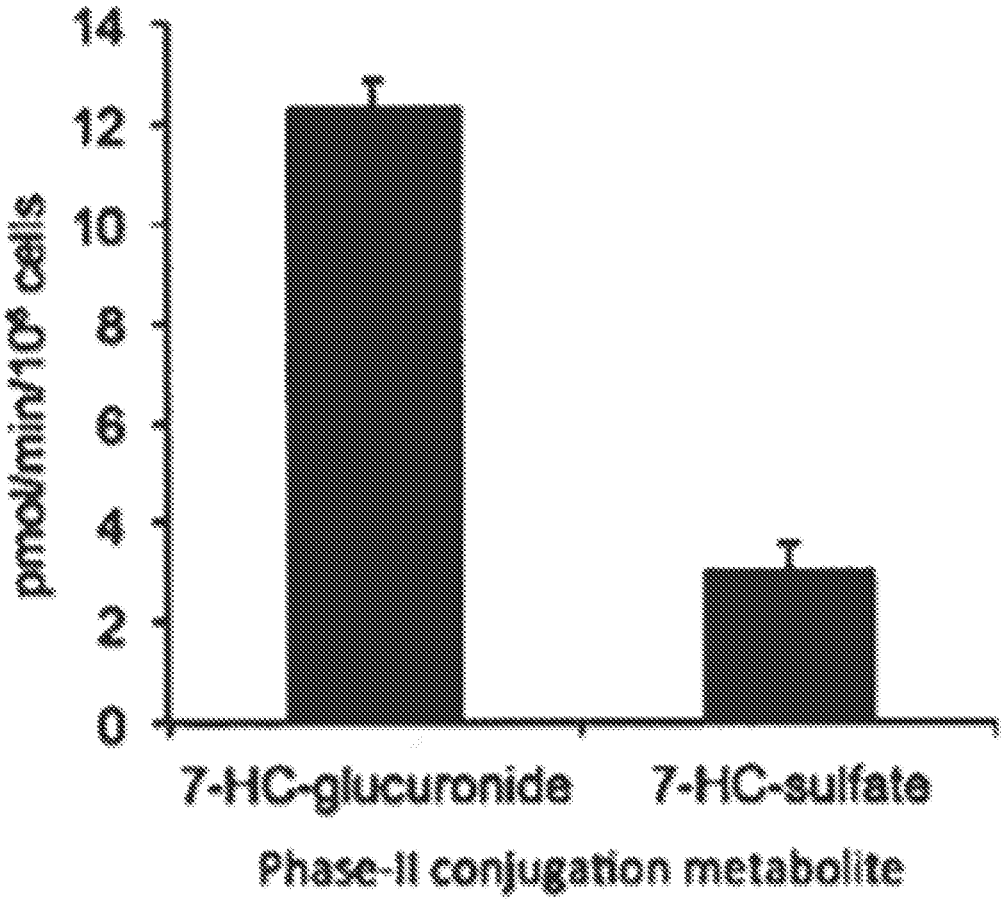
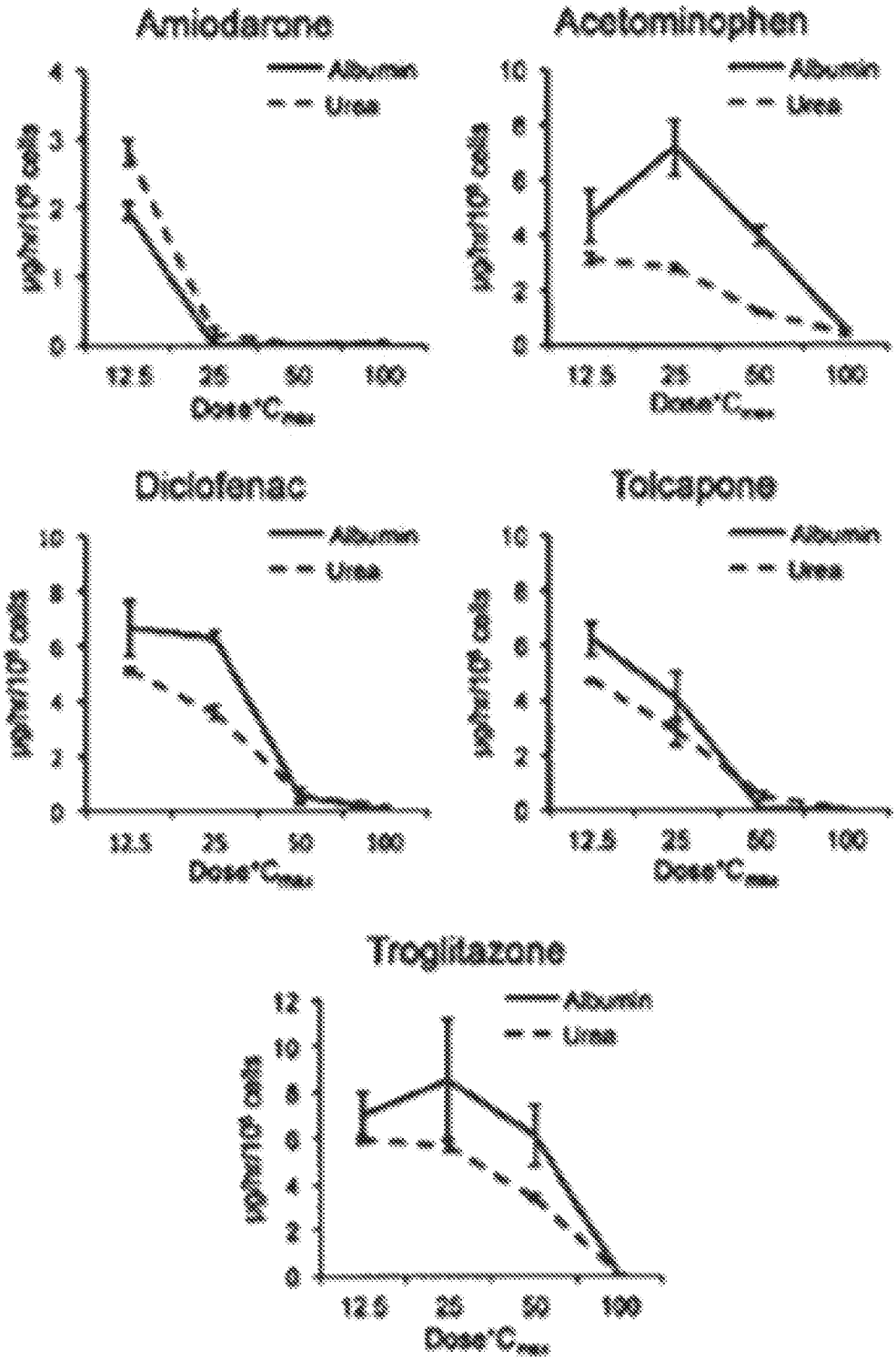

14
12
10
8
6
4
2
0
pmol/min/10^6 cells
7-HC-glucuronide
7-HC-sulfate
Phase-II conjugation metabolite

FIGURE 8

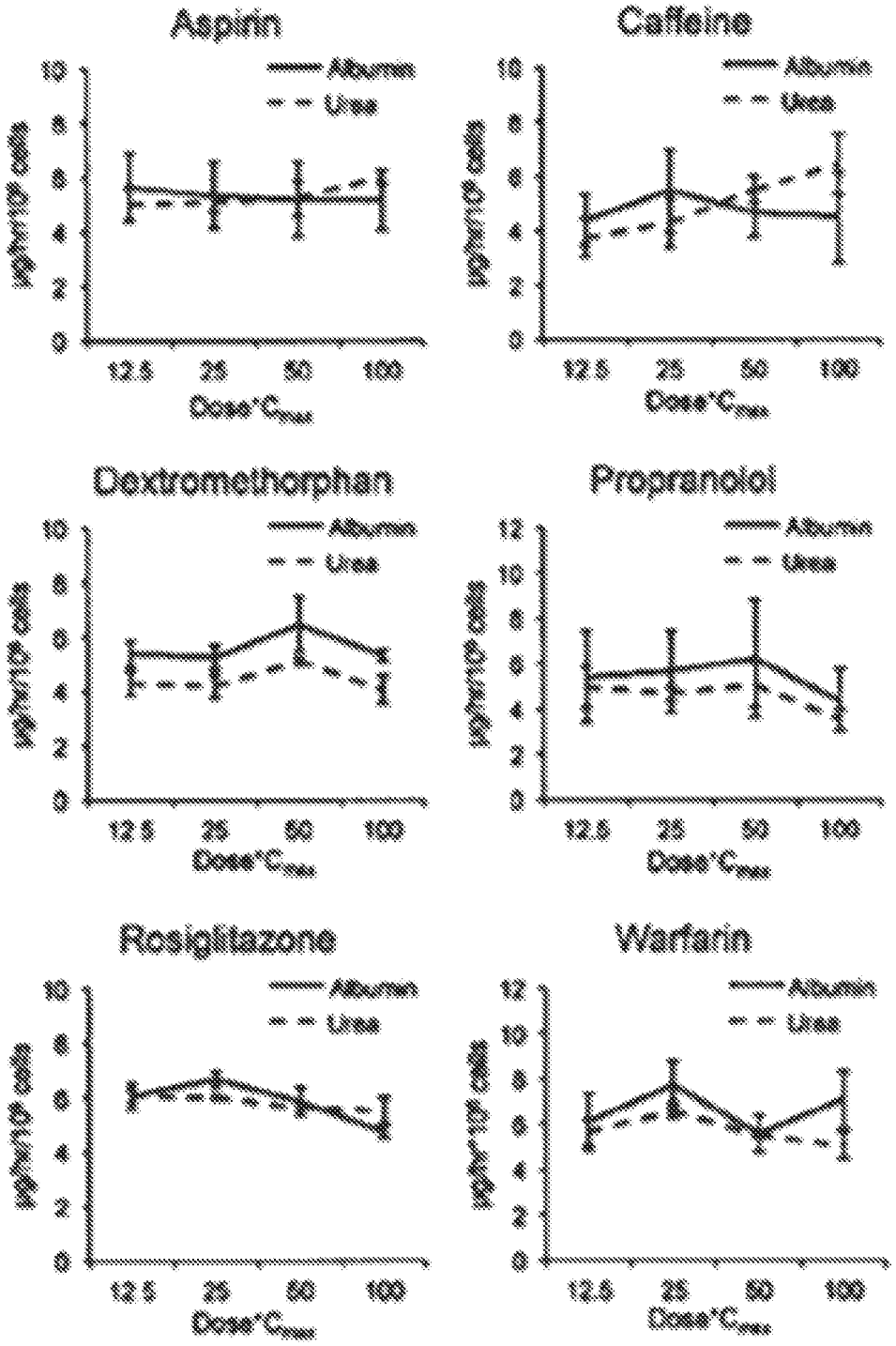
9A



Hepatotoxins

FIGURE 9A Continued

9B



Non-toxins

Continued

FIGURE 9B

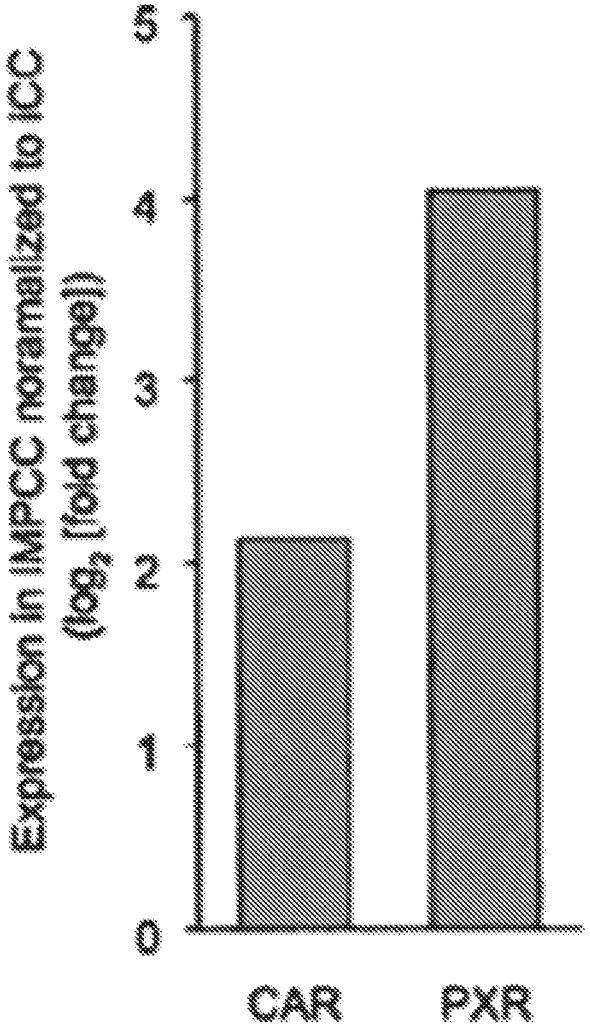

Expression in IMPCC noramalized to ICC
(log2 [fold change])
0
1
2
3
4
5
CAR
PXR

FIGURE 10

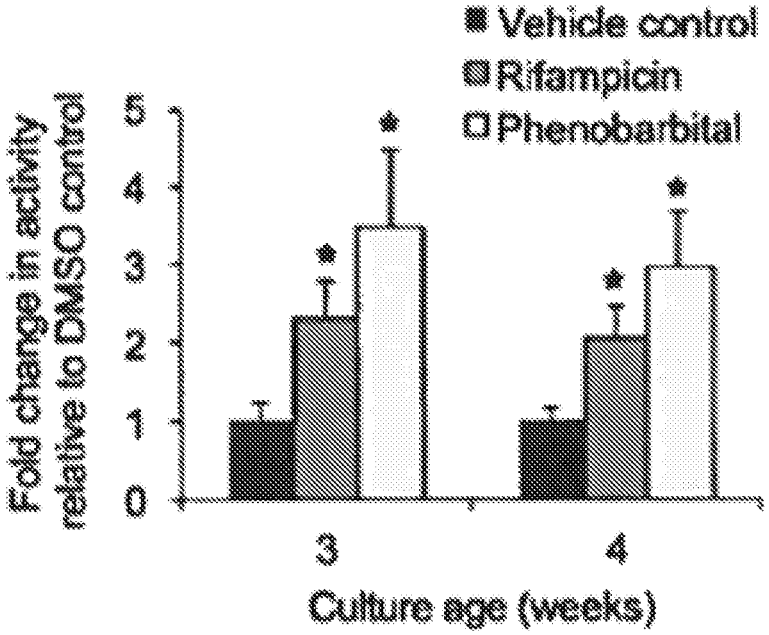
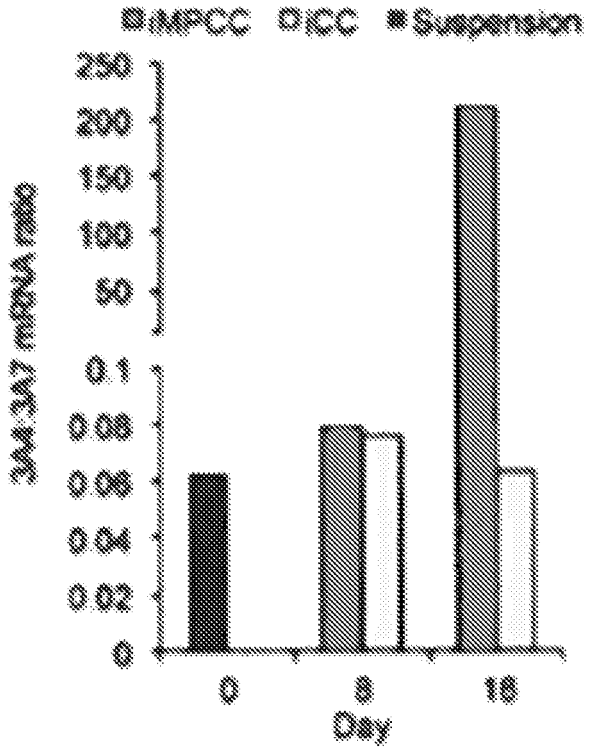

Vehicle control
Rifampicin
Phenobarbital
Fold change in activity relative to DMSO control
0
1
2
3
4
5
3
4
Culture age (weeks)

FIGURE 11

12A



12B

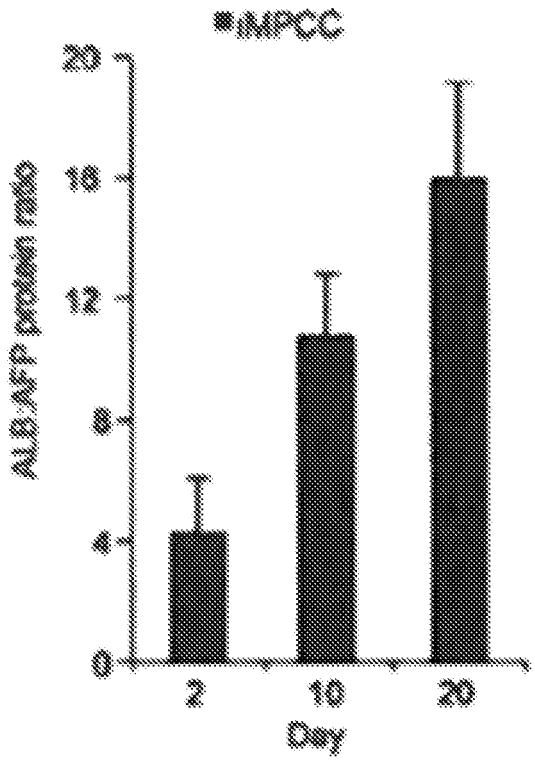


FIGURE 12A and 12B

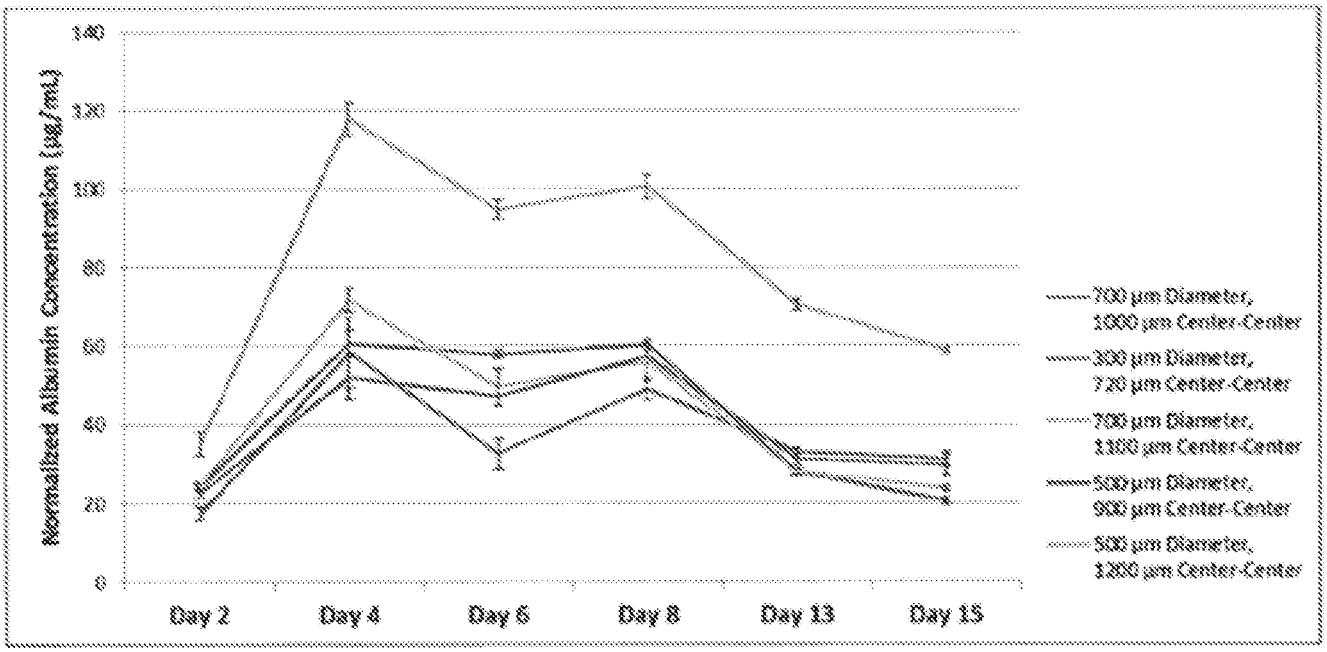

Normalized Albumin Concentration (µg/mL)
140
120
100
80
60
40
20
0
Day 2
Day 4
Day 6
Day 8
Day 13
Day 15
700 µm Diameter, 1000 µm Center-Center
300 µm Diameter, 720 µm Center-Center
700 µm Diameter, 1100 µm Center-Center
500 µm Diameter, 900 µm Center-Center
500 µm Diameter, 1200 µm Center-Center

FIGURE 13

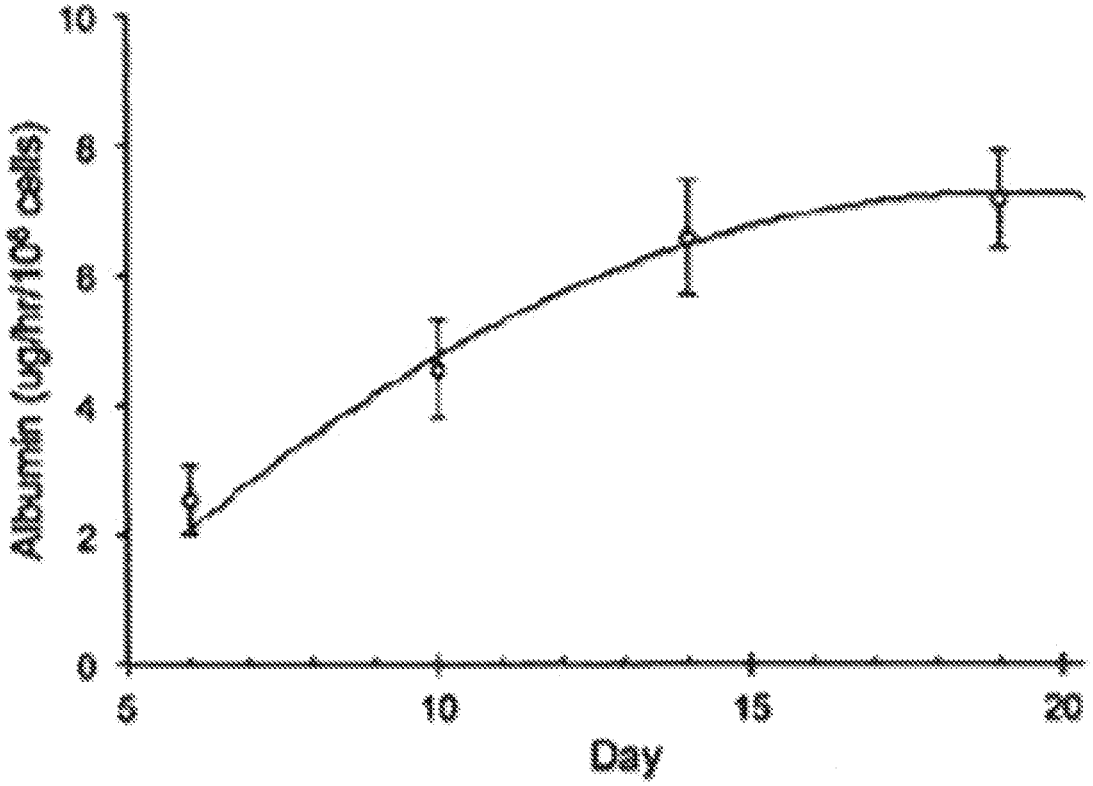
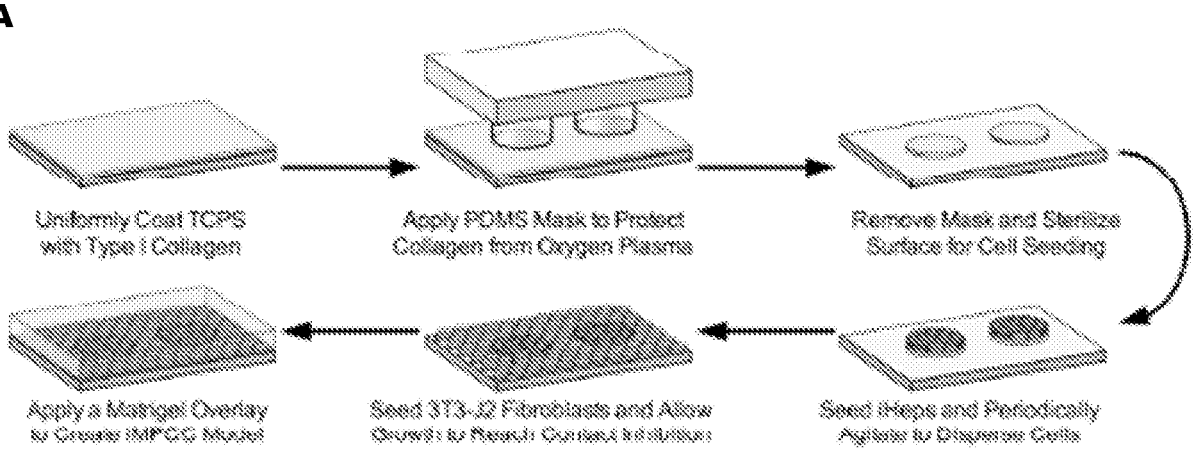
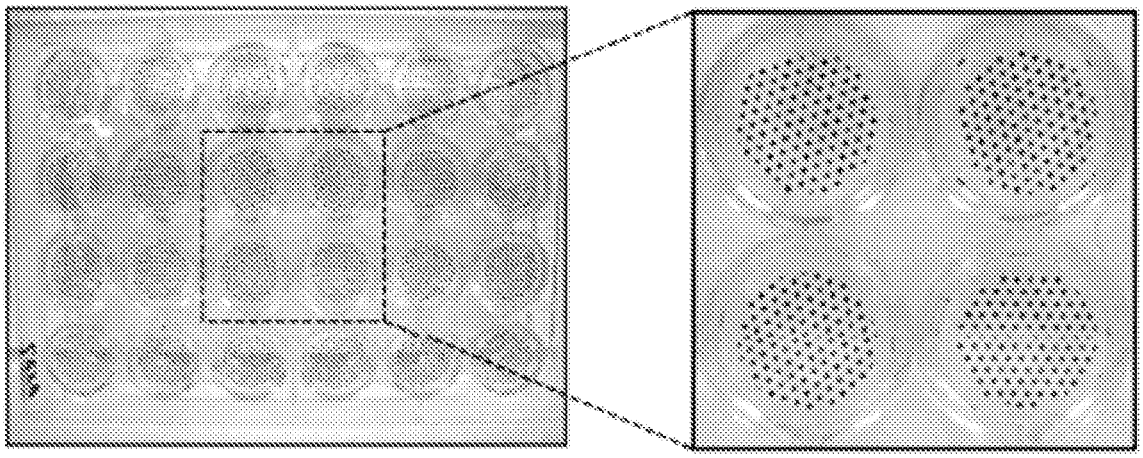


FIGURE 14

15A



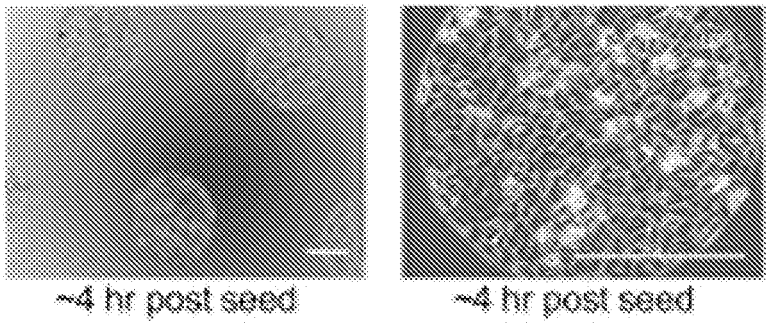
15B



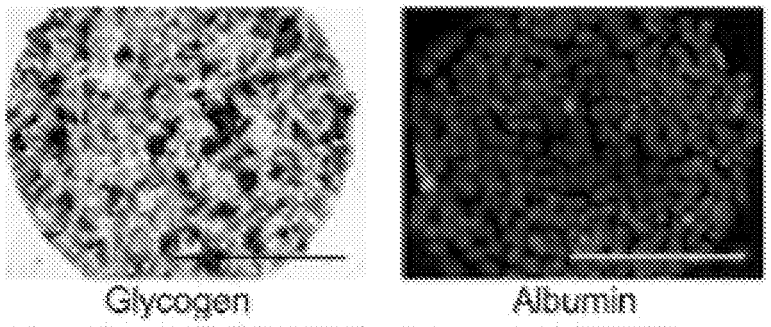
239x190mm (300 x 300 DPI)

FIGURE 15A and 15B

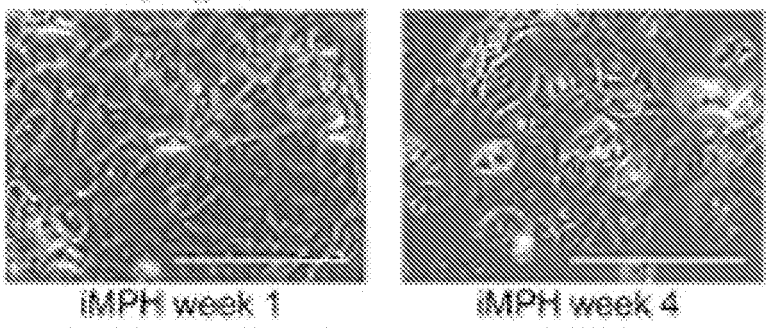
16A

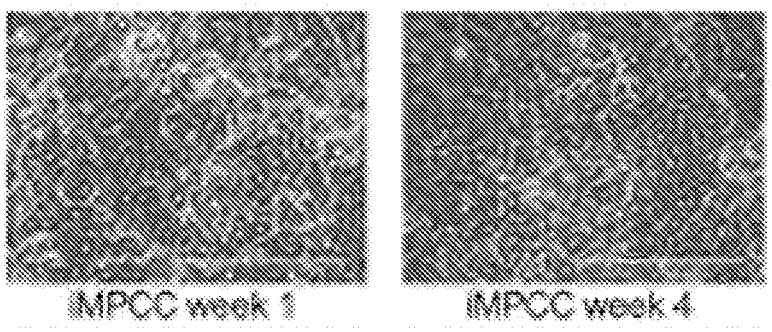


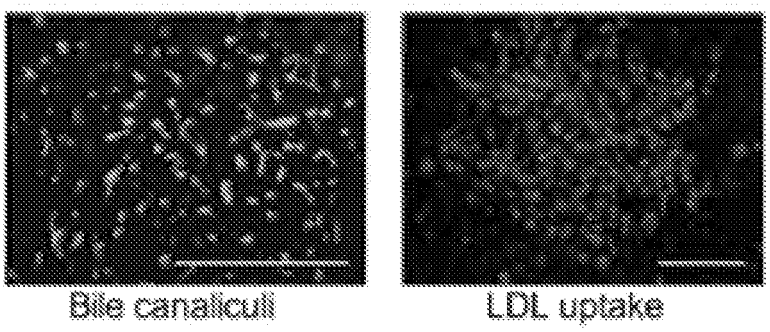
16B



16C



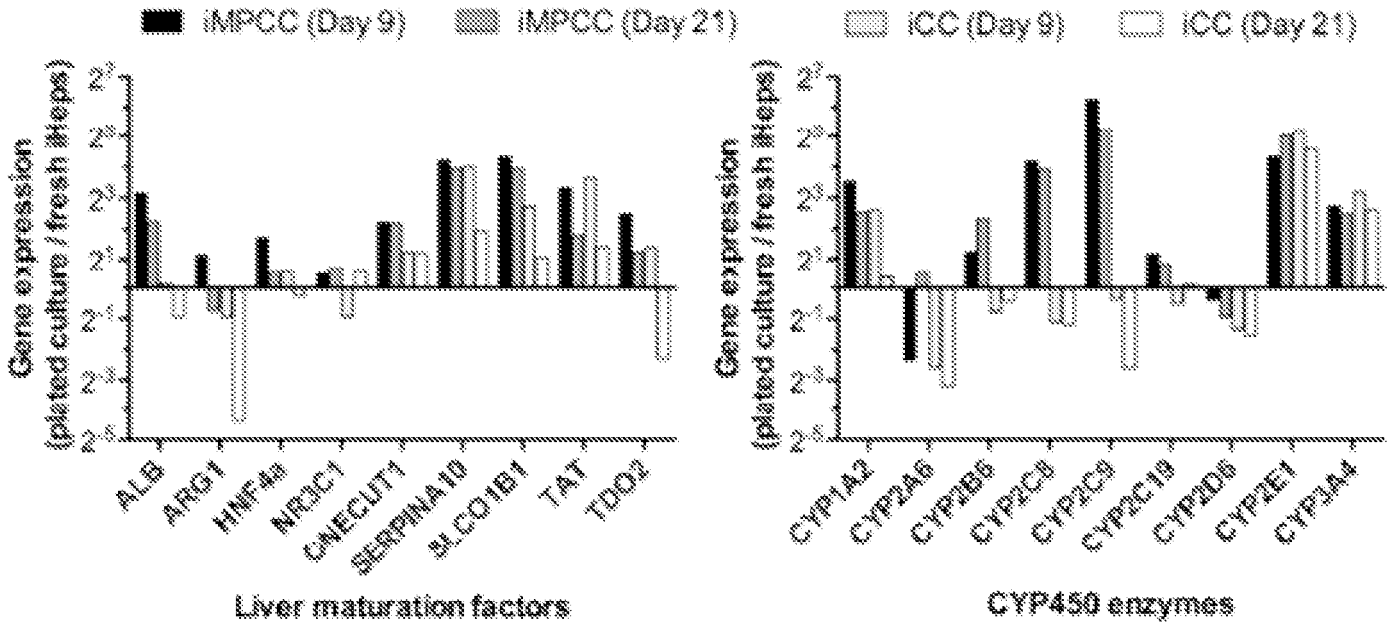




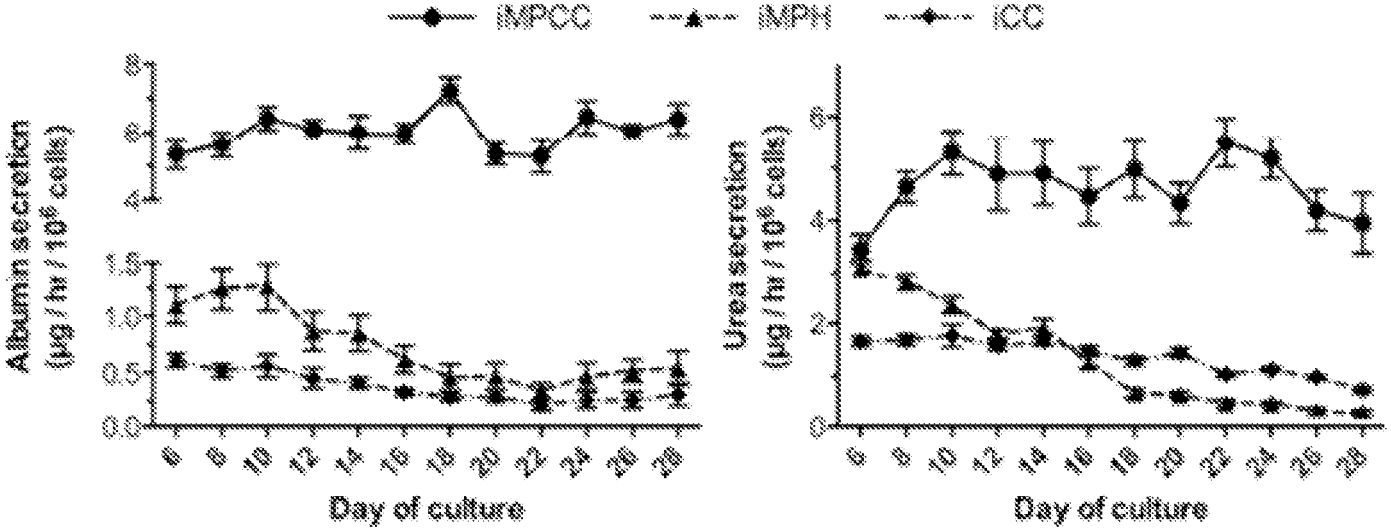
117x242mm (300 x 300 DPI)

FIGURE 16A, 16B, 16C

17A



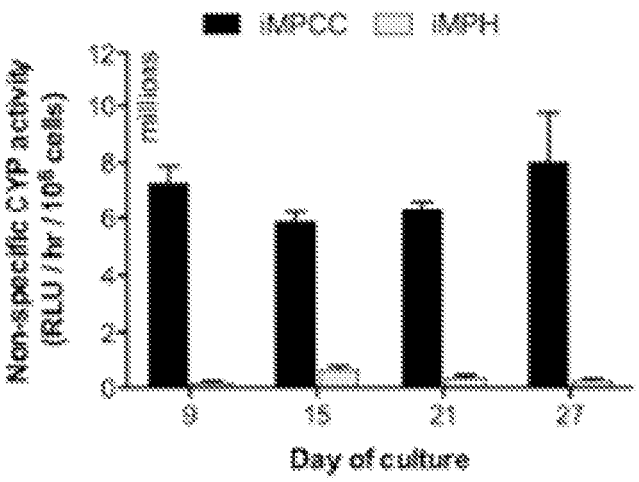
17B



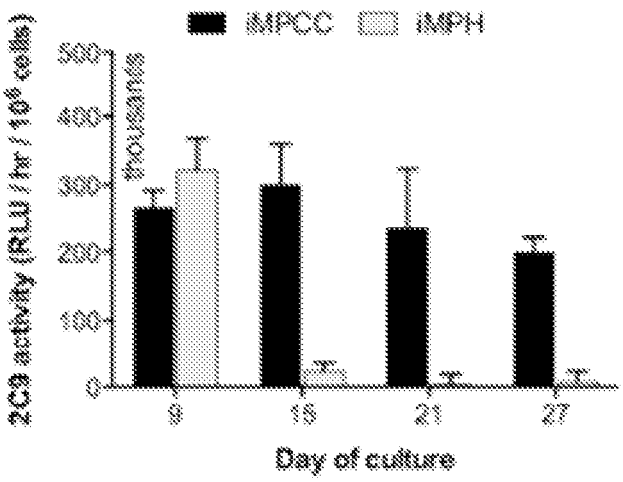
170x164mm (300 x 300 DPI)

FIGURE 17A and 17B

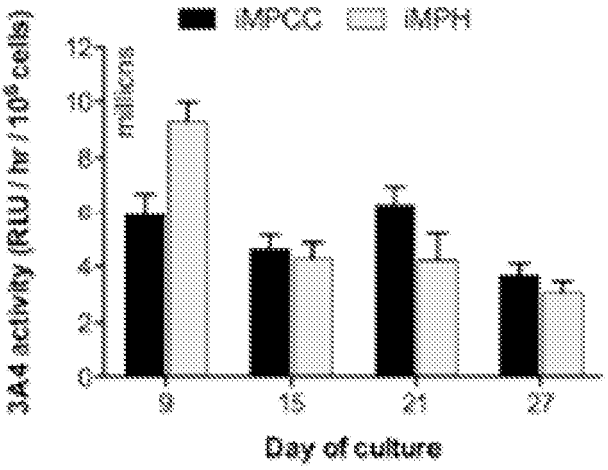
18A



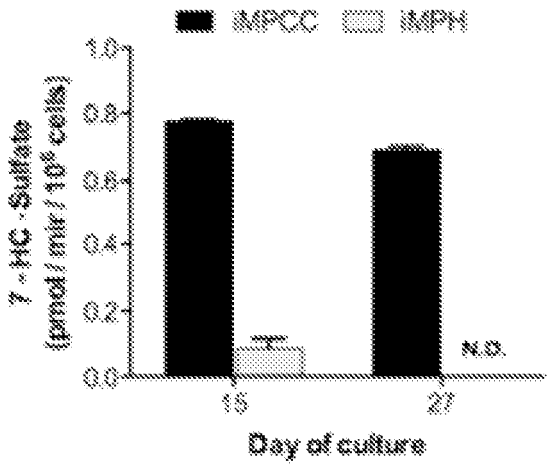
18B



18C

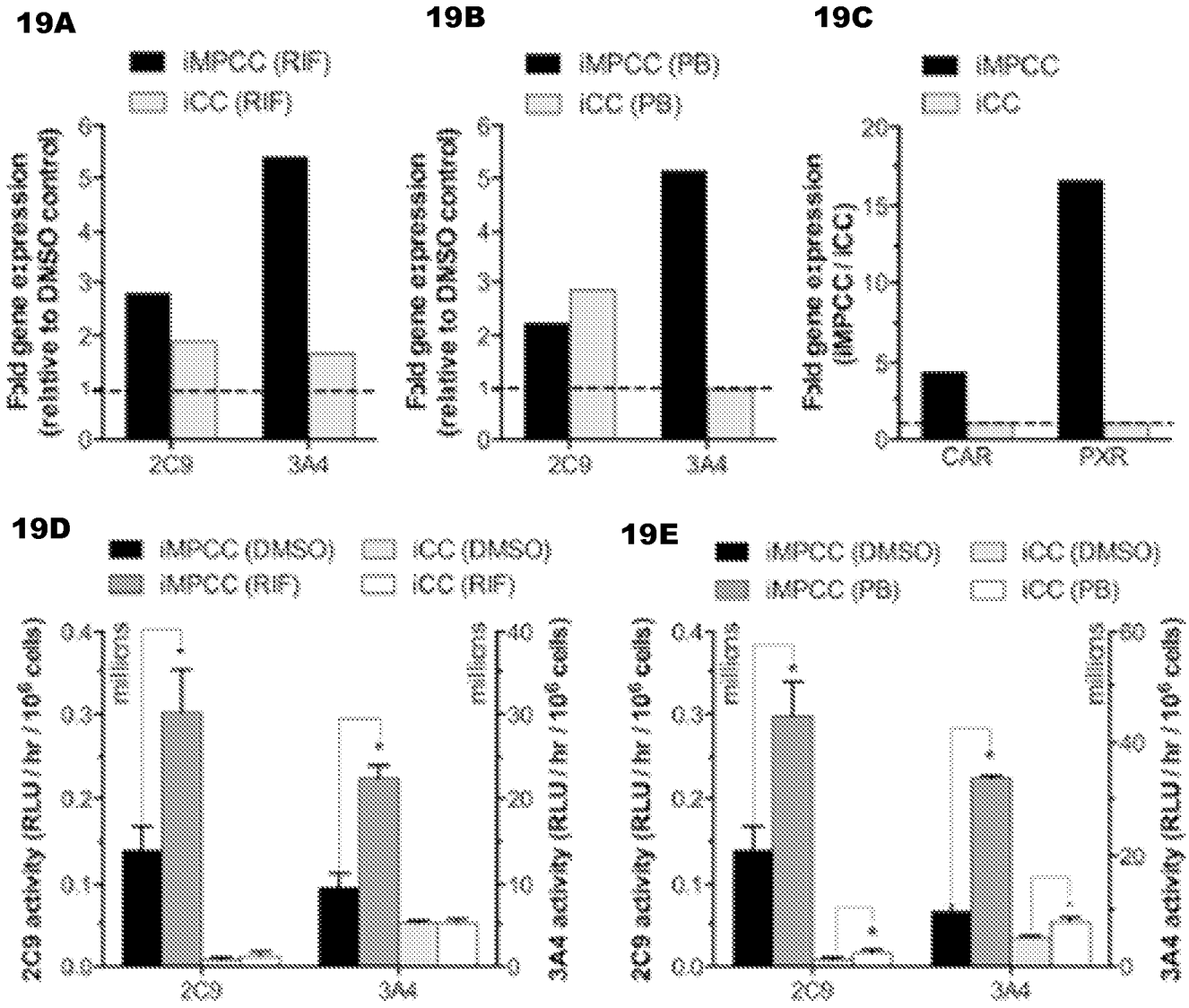


18D



162x140mm (300 x 300 DPI)

FIGURE 18A, 18B, 18C and 18D



191x178mm (300 x 300 DPI)

FIGURE 19A, 19B, 19C, 19D and 19E

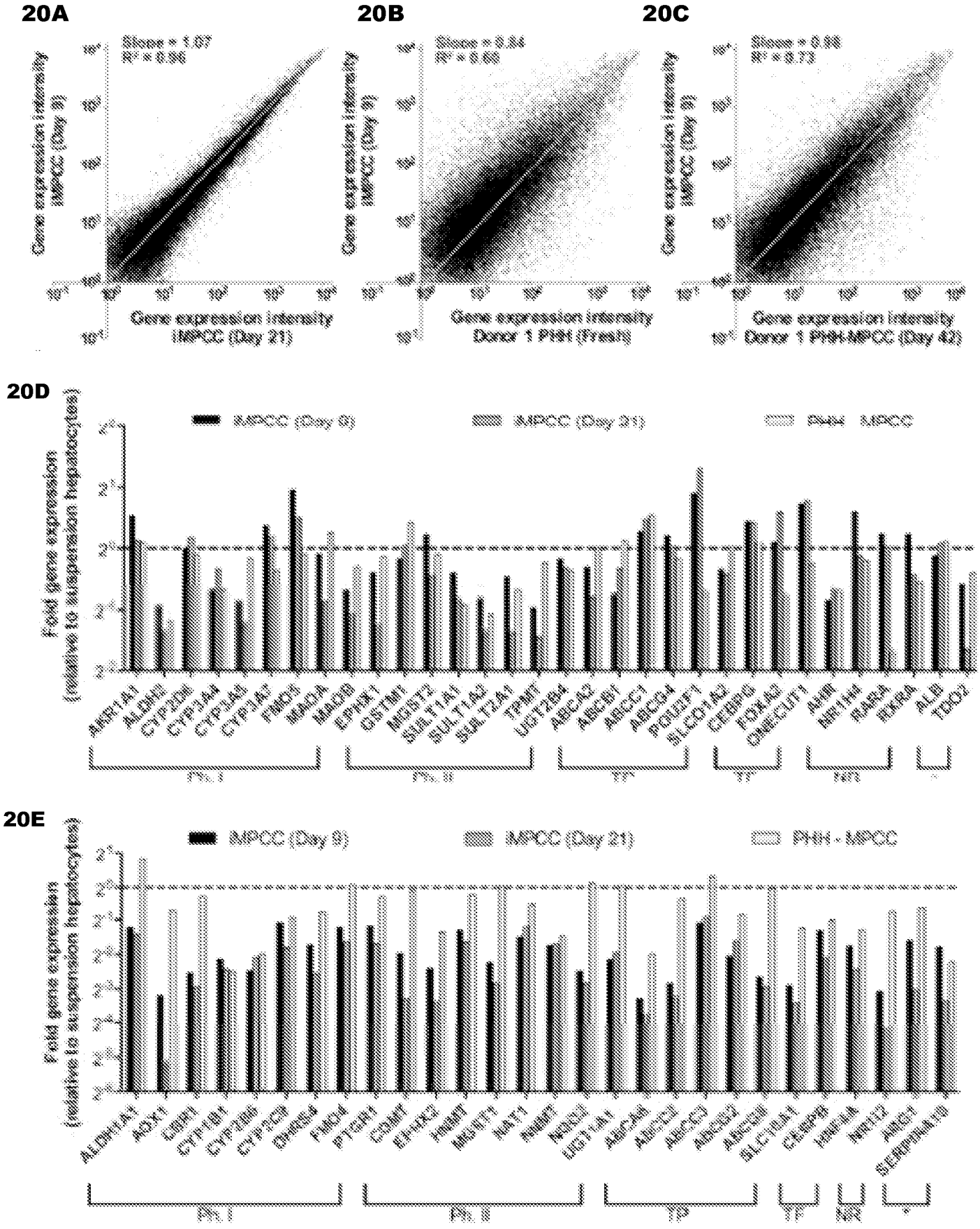
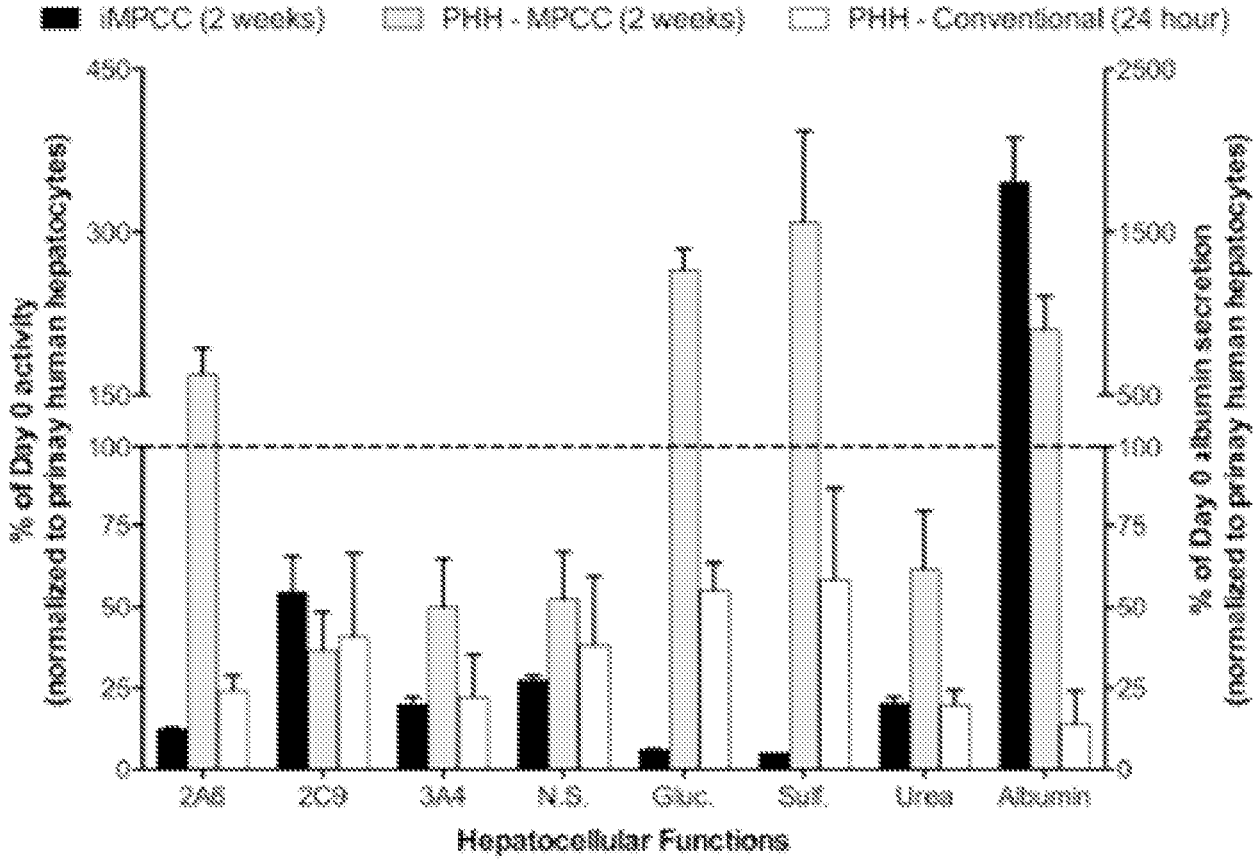
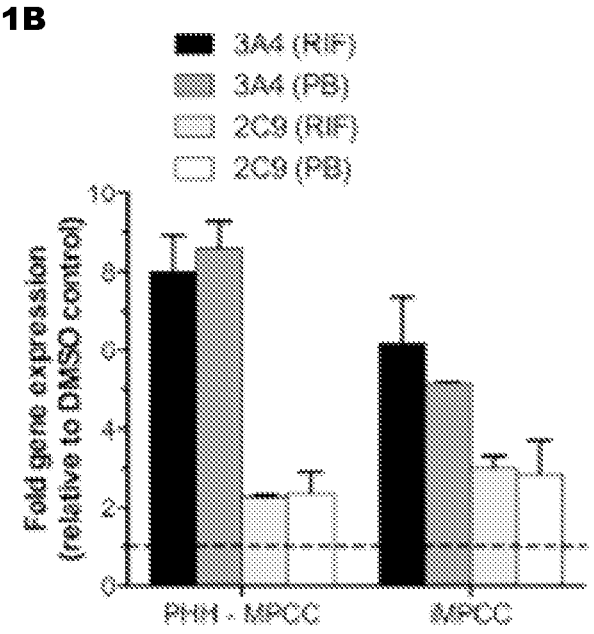


FIGURE 20A, 20B, 20C, 20D and 20E

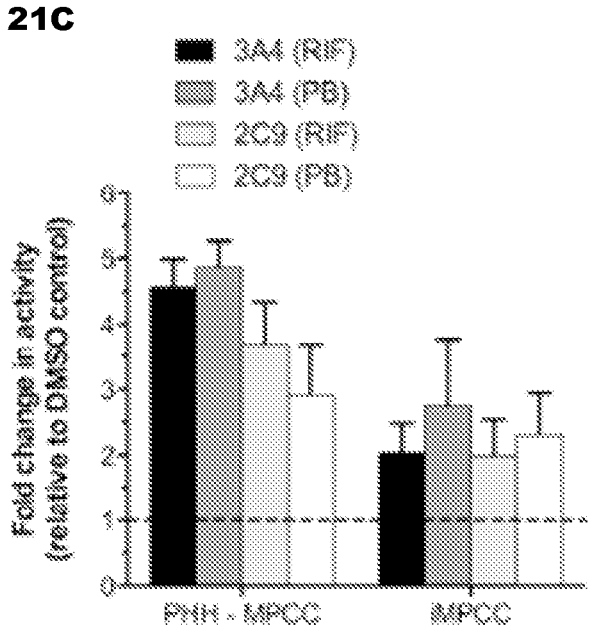
21A



21B



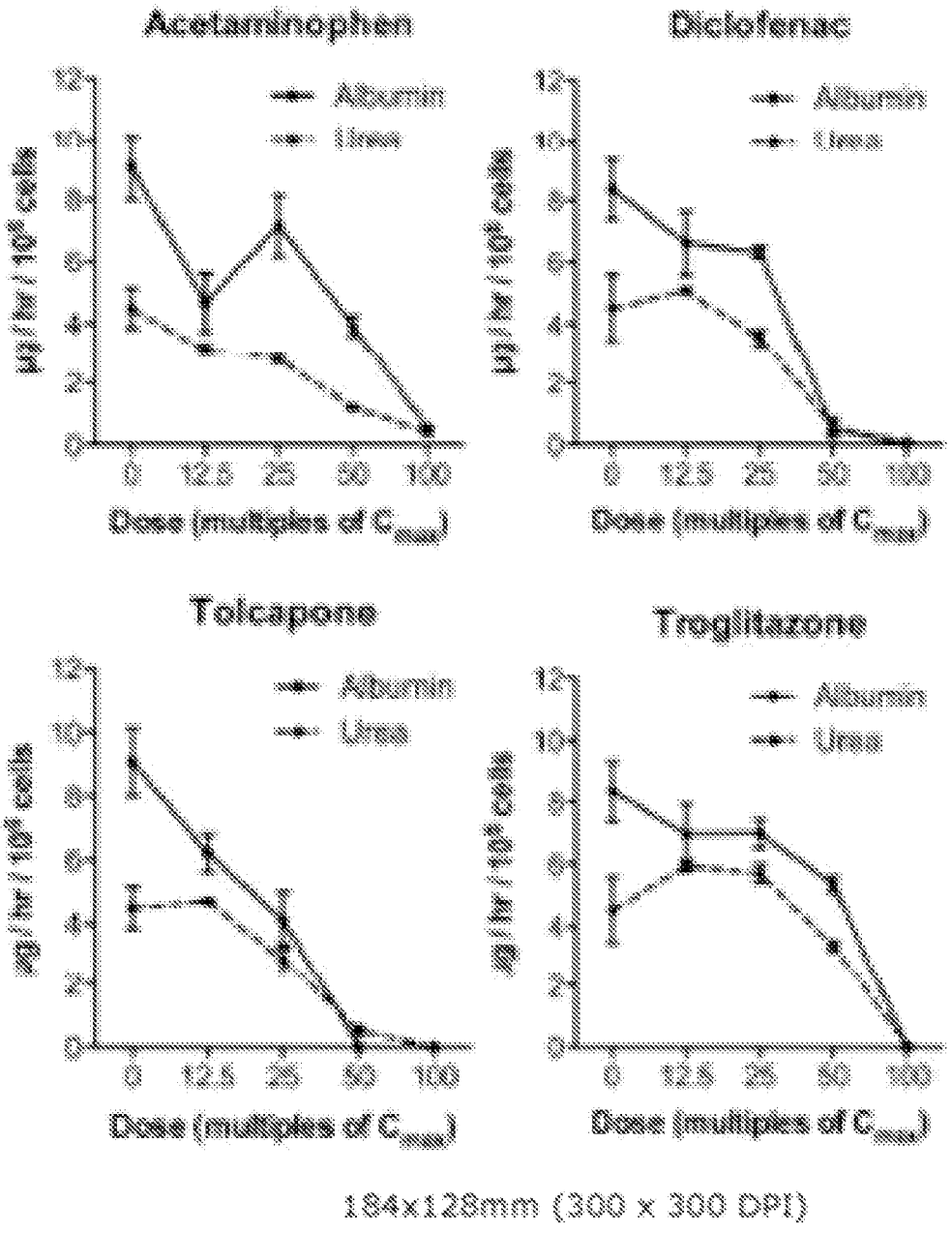
21C



171x226mm (300 x 300 DPI)

FIGURE 21A, 21B and 21C

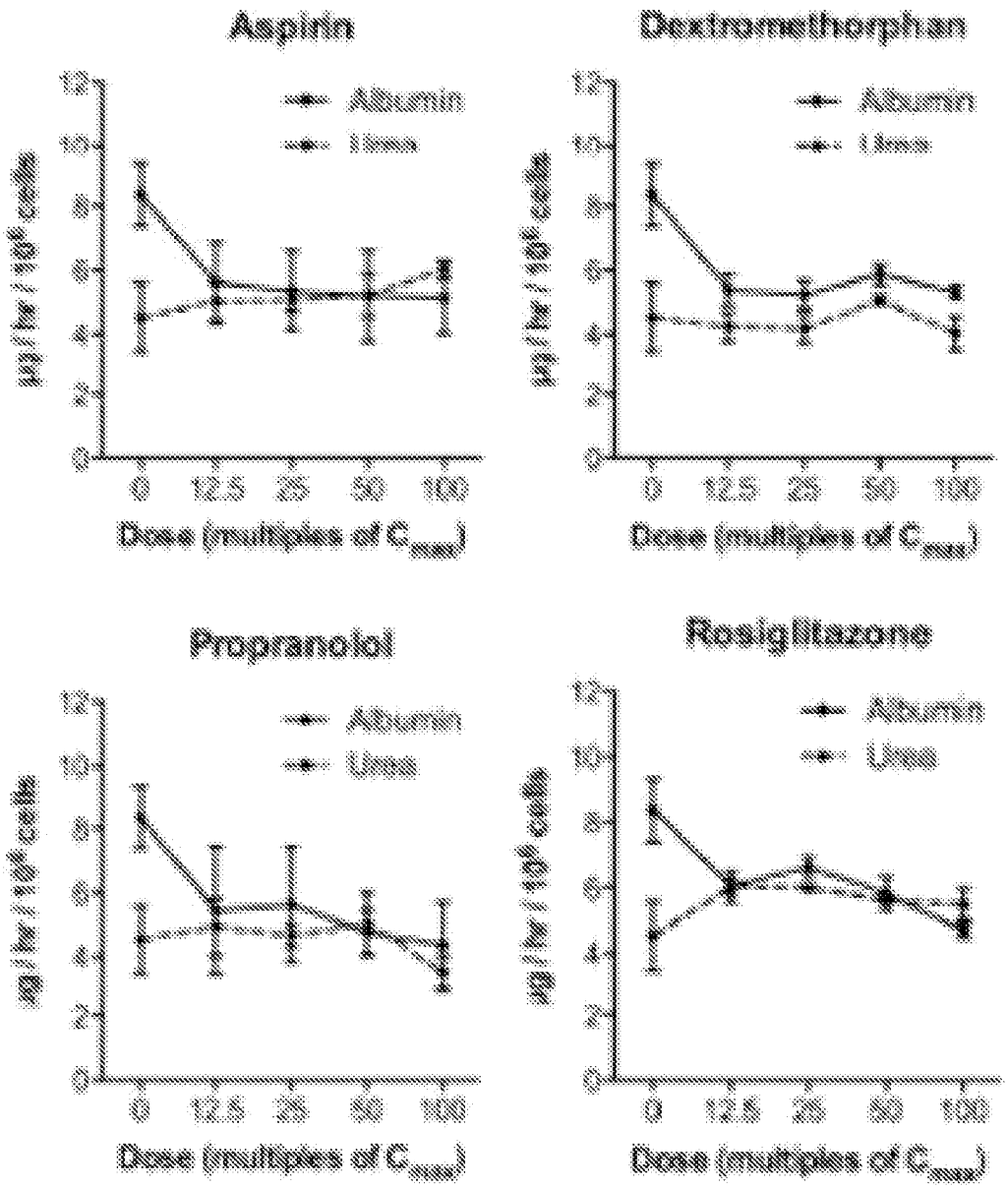
22A



184x128mm (300 x 300 DPI)

FIGURE 22A
Continued

22B



184x128mm (300 x 300 DPI)

Continued
FIGURE 22B

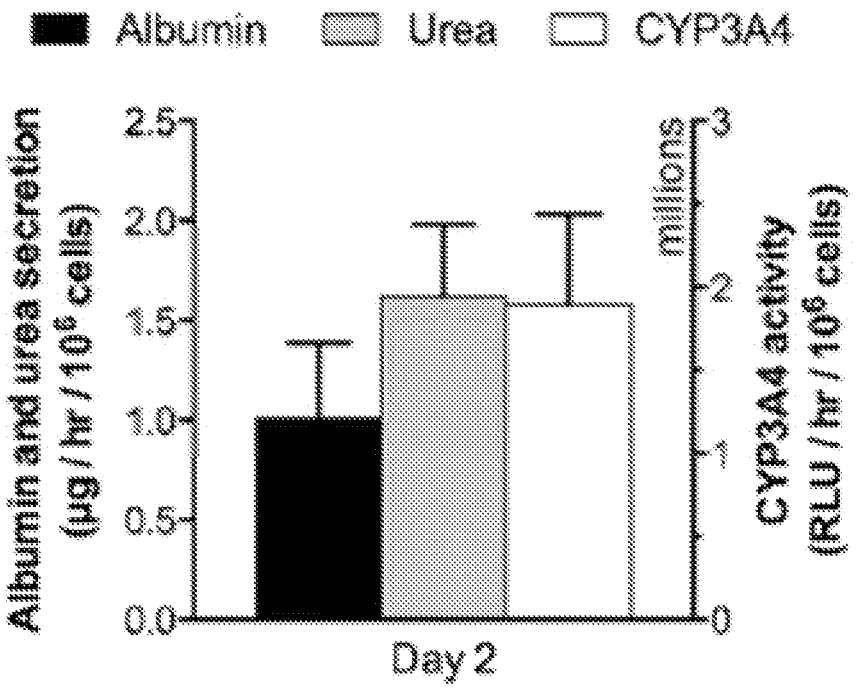

Albumin
Urea
CYP3A4
Albumin and urea secretion (µg / hr / 10^6 cells)
2.5
2.0
1.5
1.0
0.5
0.0
millions
3
2
1
0
CYP3A4 activity (RLU / hr / 10^6 cells)
Day 2

FIGURE 23

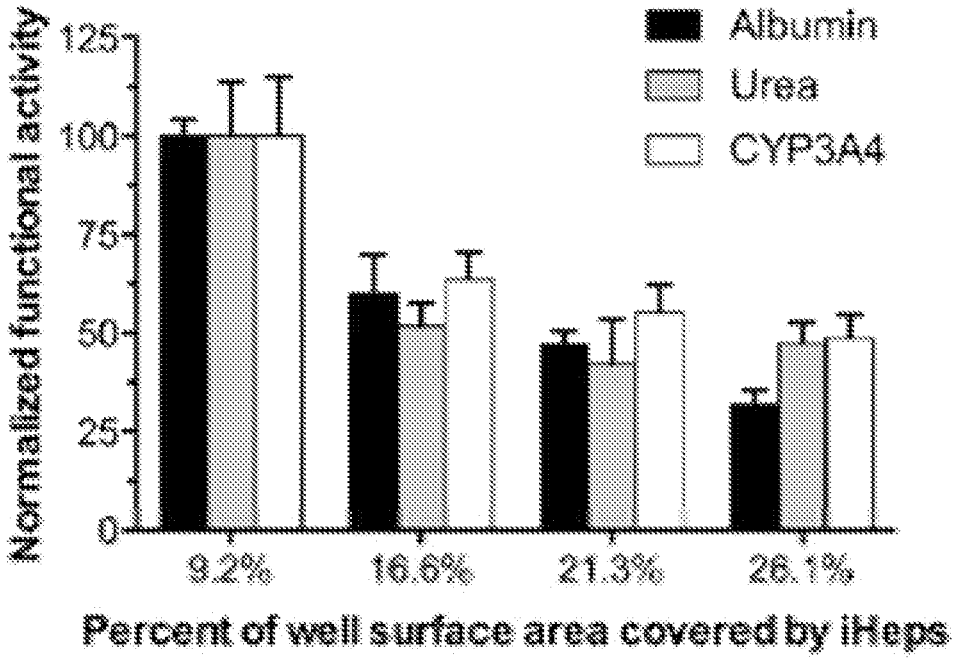

Albumin
Urea
CYP3A4
Normalized functional activity
125
100
75
50
25
0
9.2%
16.6%
21.3%
26.1%
Percent of well surface area covered by iHeps

FIGURE 24

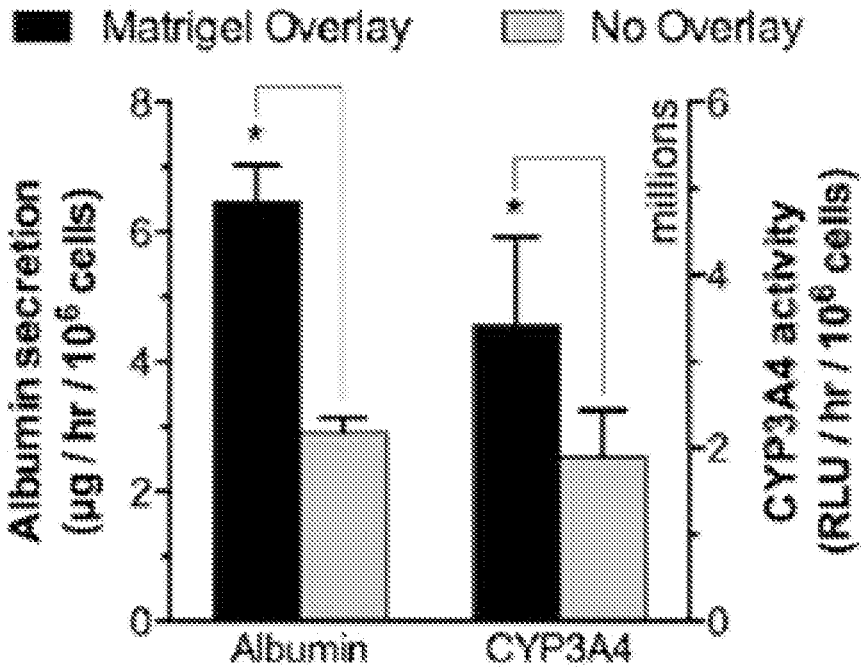
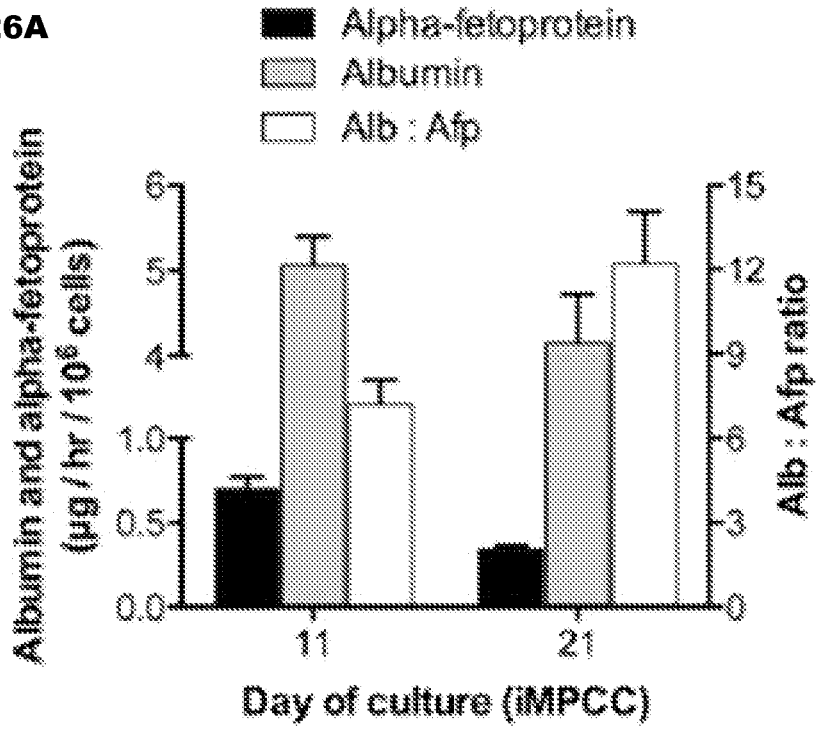

Matrigel Overlay
No Overlay
Albumin secretion (µg / hr / 10^6 cells)
CYP3A4 activity (RLU / hr / 10^6 cells)
millions
0
2
4
6
8
Albumin
CYP3A4
*
*

FIGURE 25

26A



26B

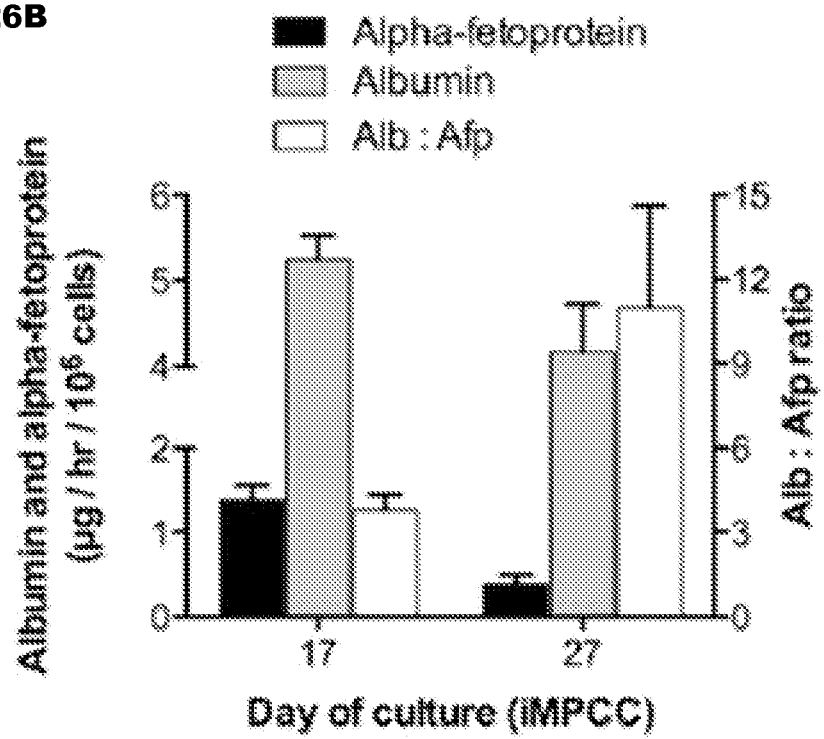


FIGURE 26A and 26B

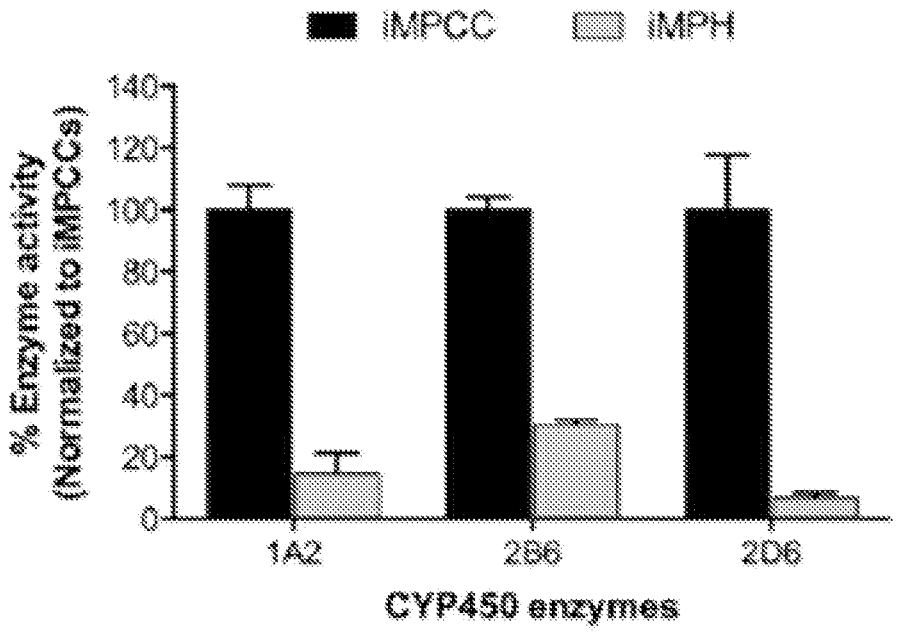
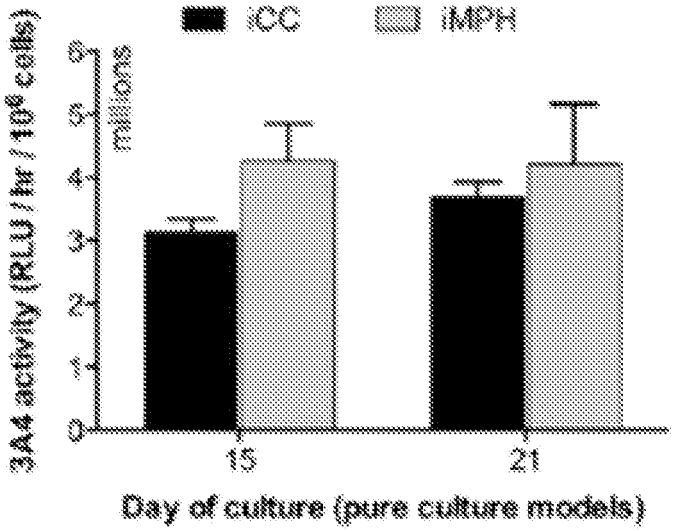
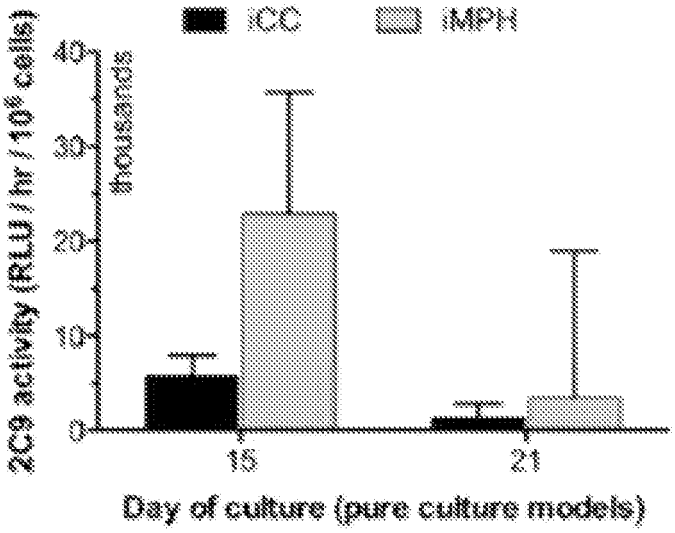

IMPCC
IMPH
% Enzyme activity
(Normalized to IMPCCs)
140
120
100
80
60
40
20
0
1A2
2B6
2D6
CYP450 enzymes

FIGURE 27

28A



28B



28C

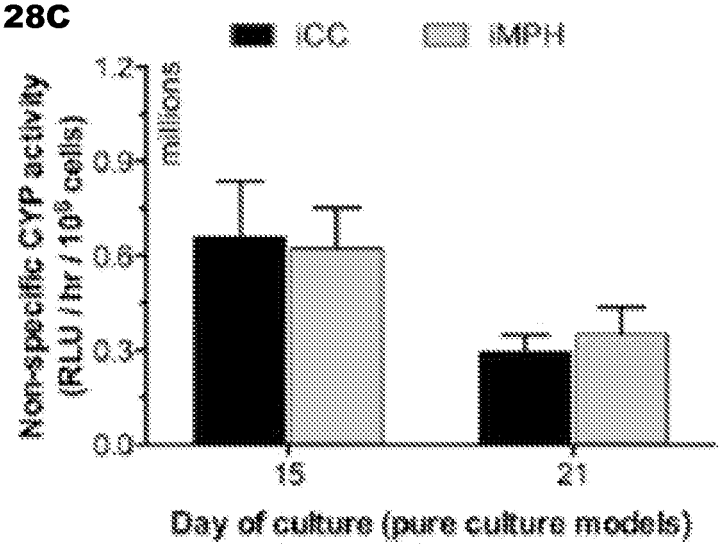


FIGURE 28A, 28B, and 28C

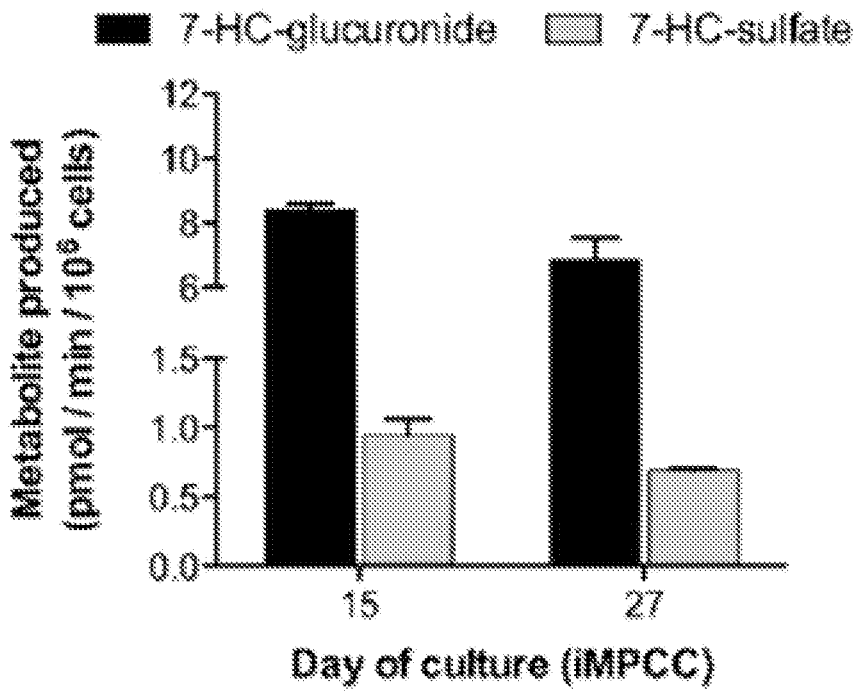
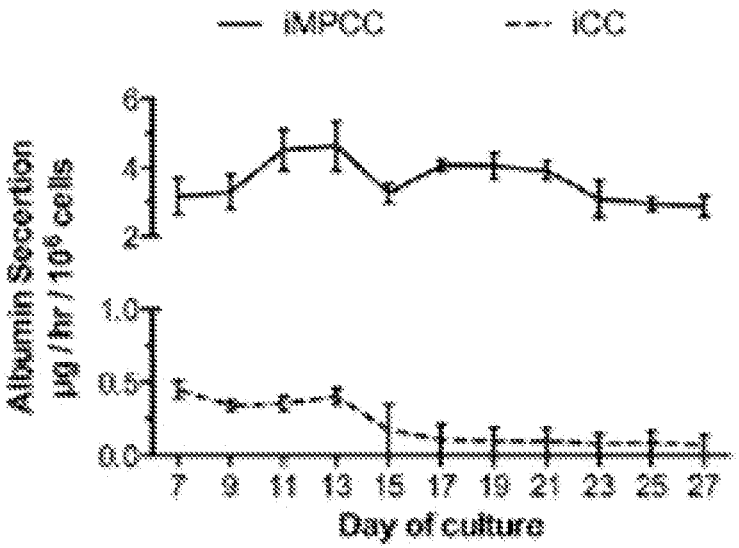

7-HC-glucuronide
7-HC-sulfate
Metabolite produced
(pmol / min / 10^6 cells)
12
10
8
6
1.5
1.0
0.5
0.0
15
27
Day of culture (iMPCC)

FIGURE 29

30A



30B

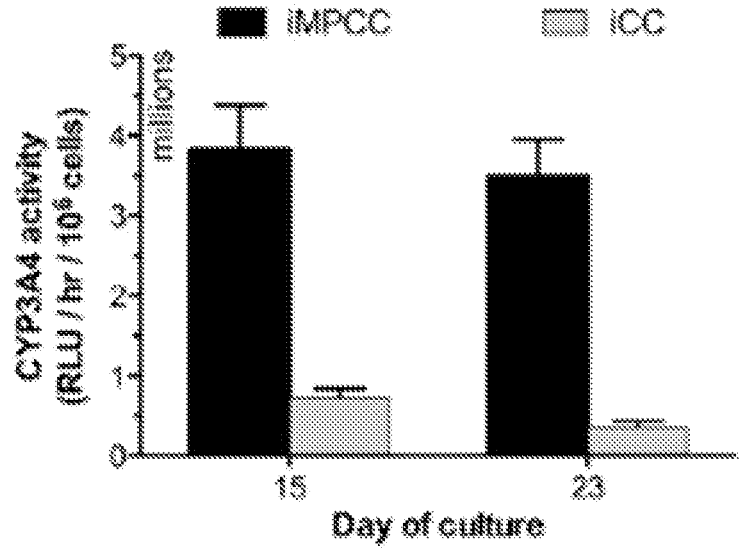
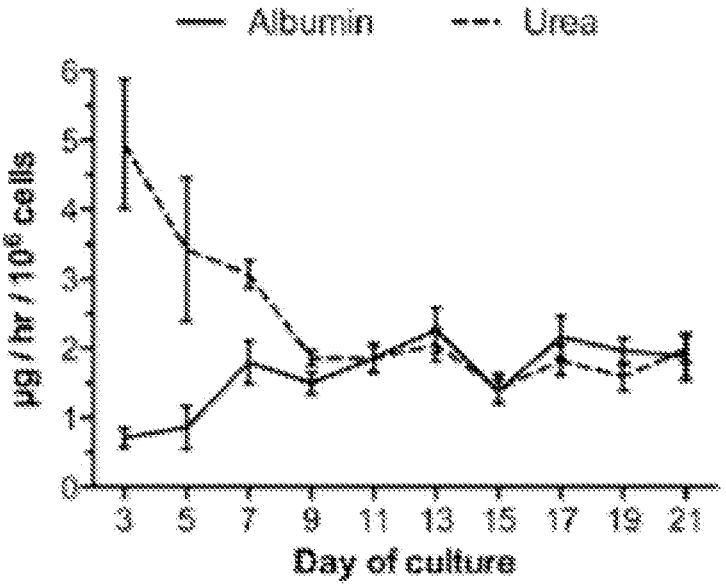


FIGURE 30A and 30B

31A



31B

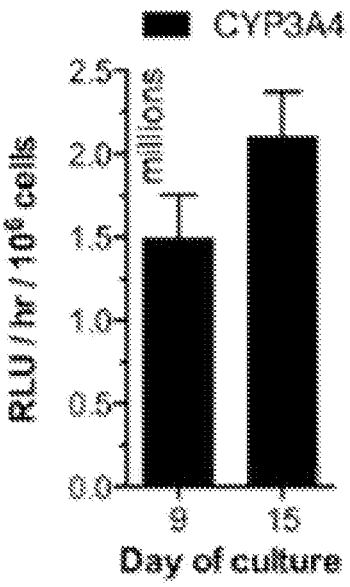


FIGURE 31A and 31B

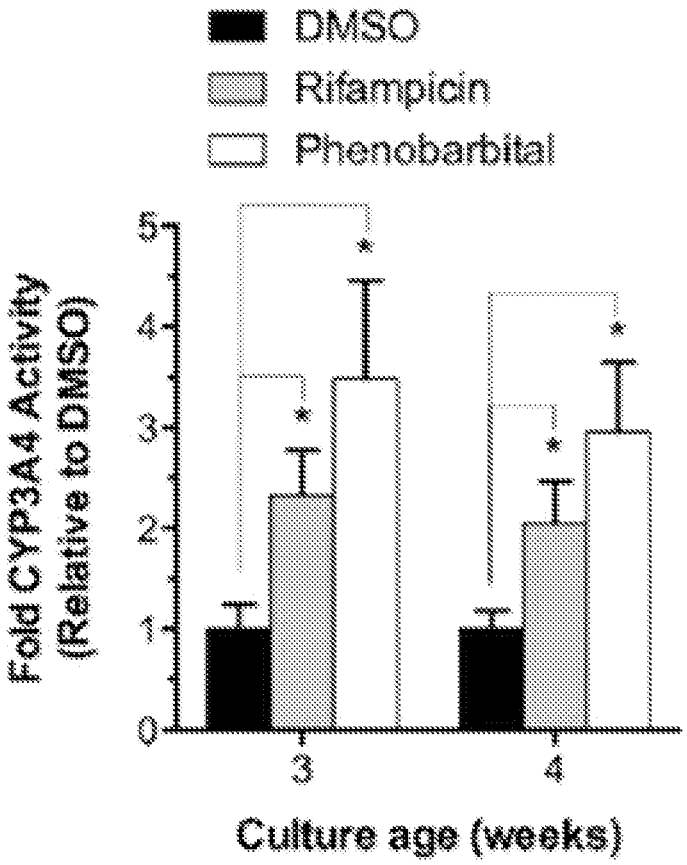

DMSO
Rifampicin
Phenobarbital
Fold CYP3A4 Activity
(Relative to DMSO)
0
1
2
3
4
5
*
*
*
*
3
4
Culture age (weeks)

FIGURE 32

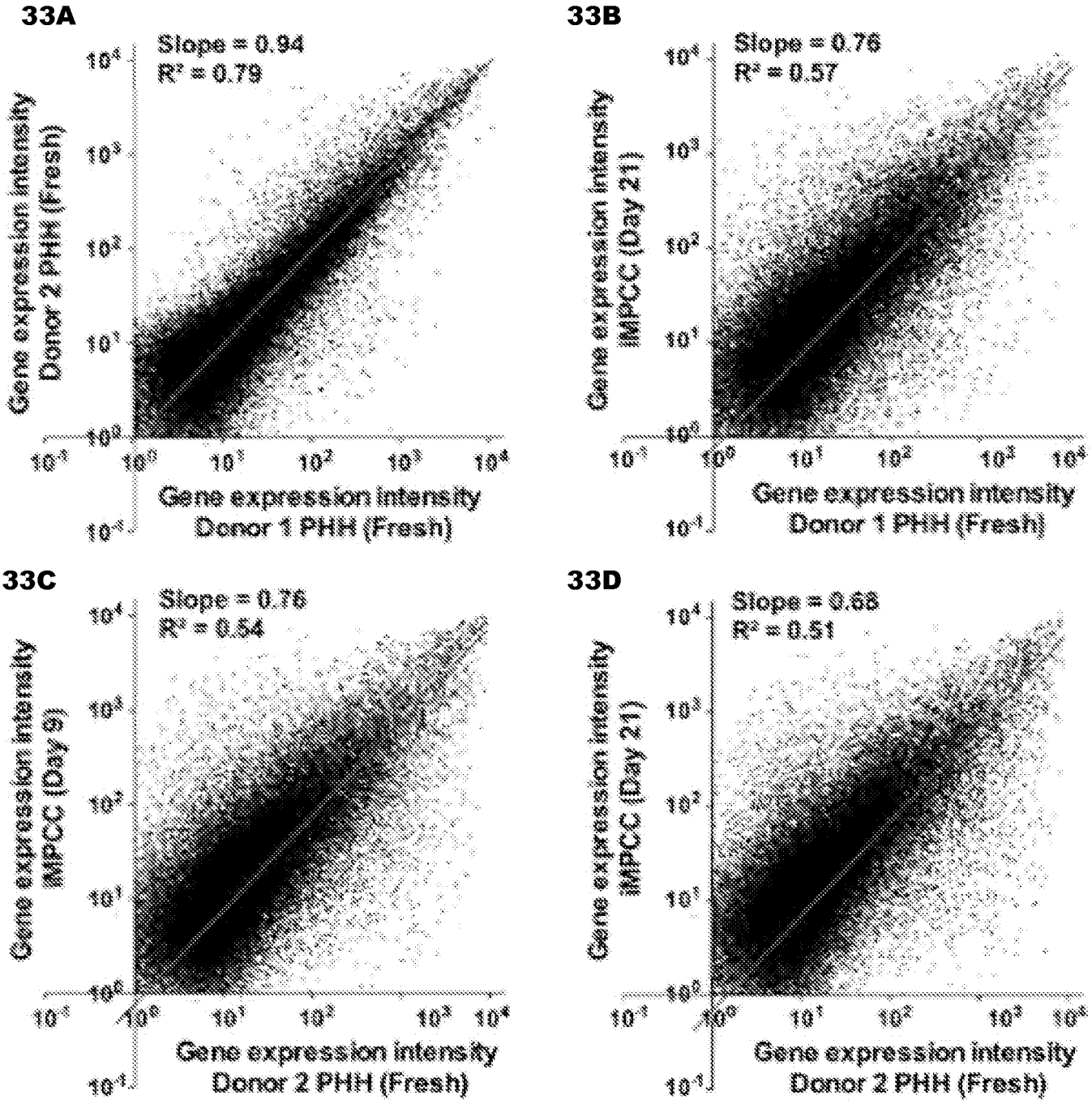


FIGURE 33A, 33B, 33C and 33D

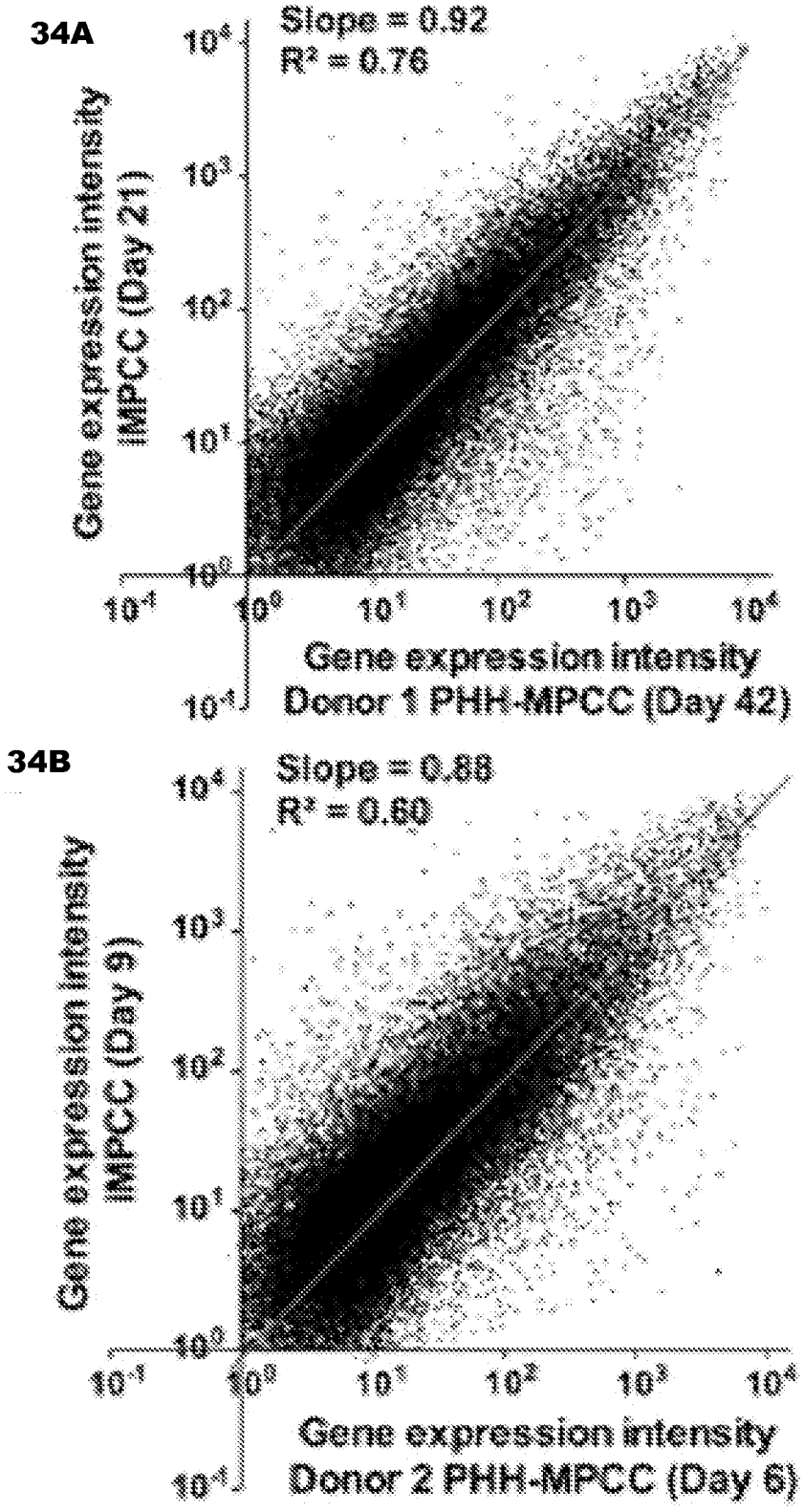
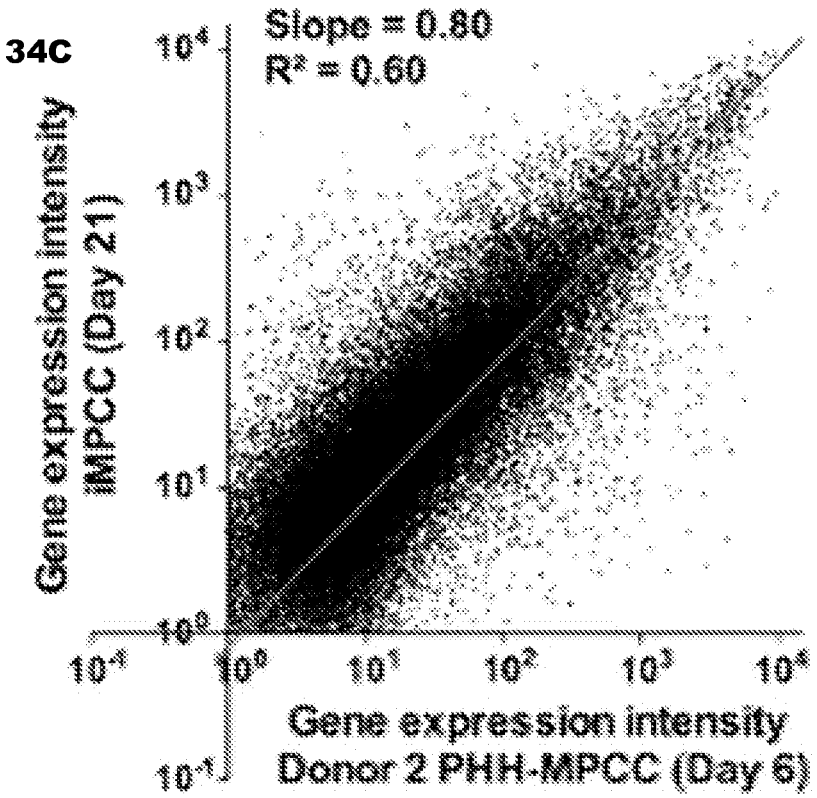


FIGURE 34A and 34C Continued



Continue
FIGURE 34C

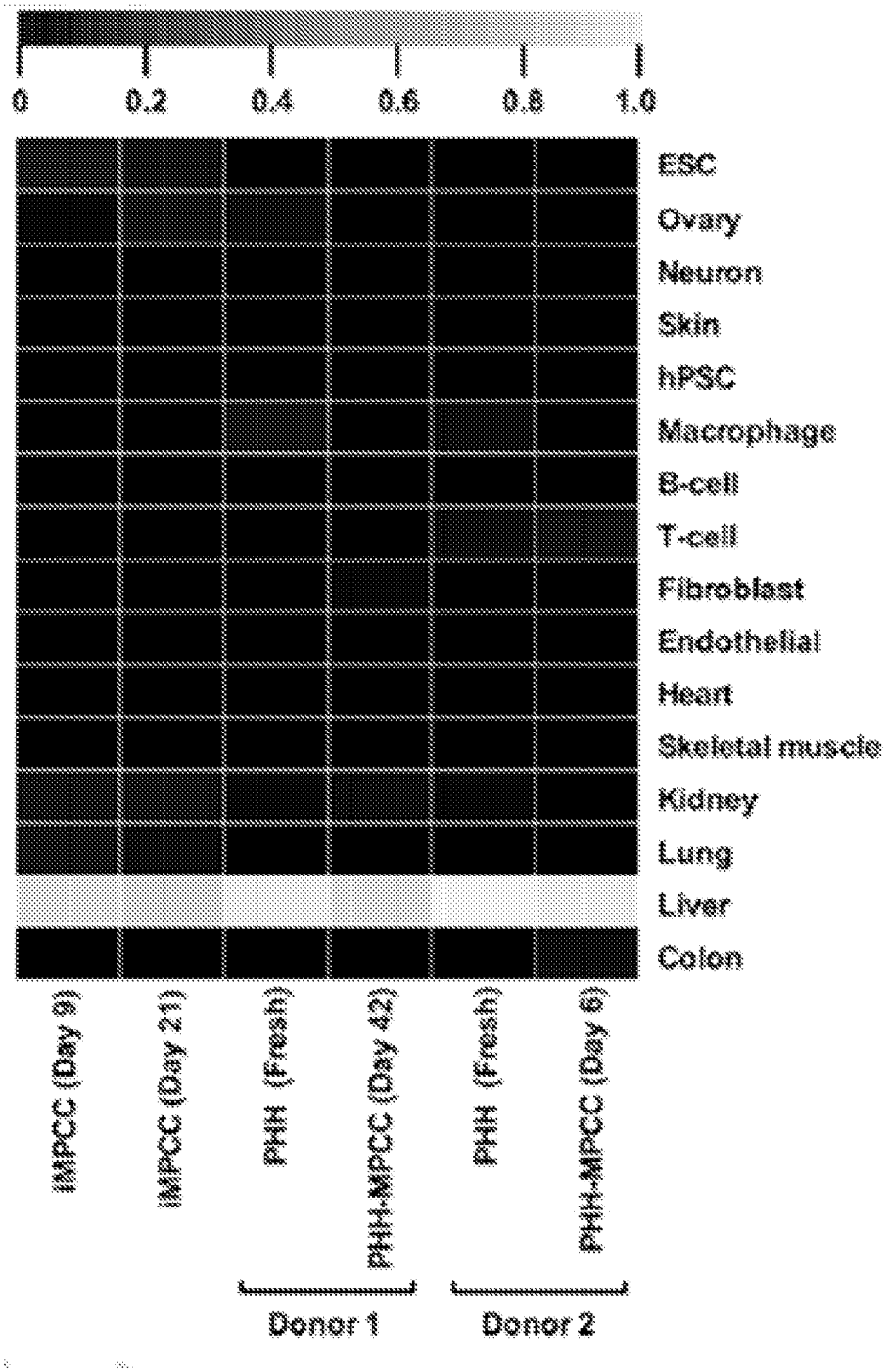

0
0.2
0.4
0.6
0.8
1.0
ESC
Ovary
Neuron
Skin
hPSC
Macrophage
B-cell
T-cell
Fibroblast
Endothelial
Heart
Skeletal muscle
Kidney
Lung
Liver
Colon
iMPCC (Day 9)
iMPCC (Day 21)
PHH (Fresh)
PHH-MPCC (Day 42)
PHH (Fresh)
PHH-MPCC (Day 6)
Donor 1
Donor 2

FIGURE 35

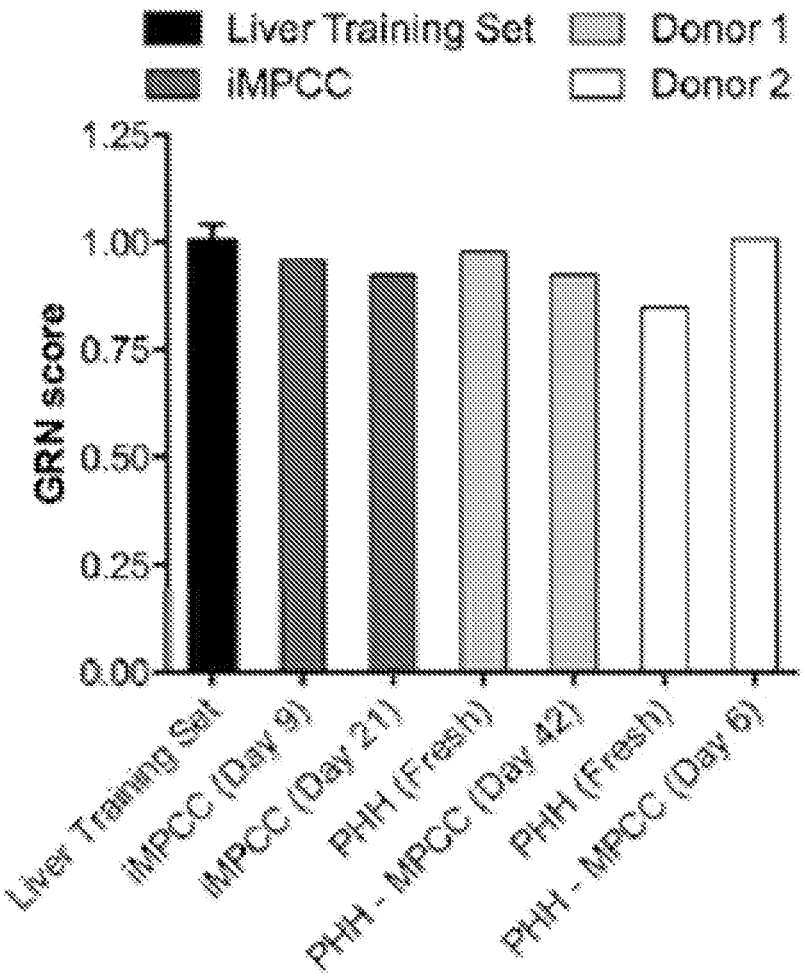

Liver Training Set
iMPCC
Donor 1
Donor 2
GRN score
1.25
1.00
0.75
0.50
0.25
0.00
Liver Training Set
iMPCC (Day 9)
iMPCC (Day 21)
PHH (Fresh)
PHH - MPCC (Day 42)
PHH (Fresh)
PHH - MPCC (Day 6)

FIGURE 36

37A

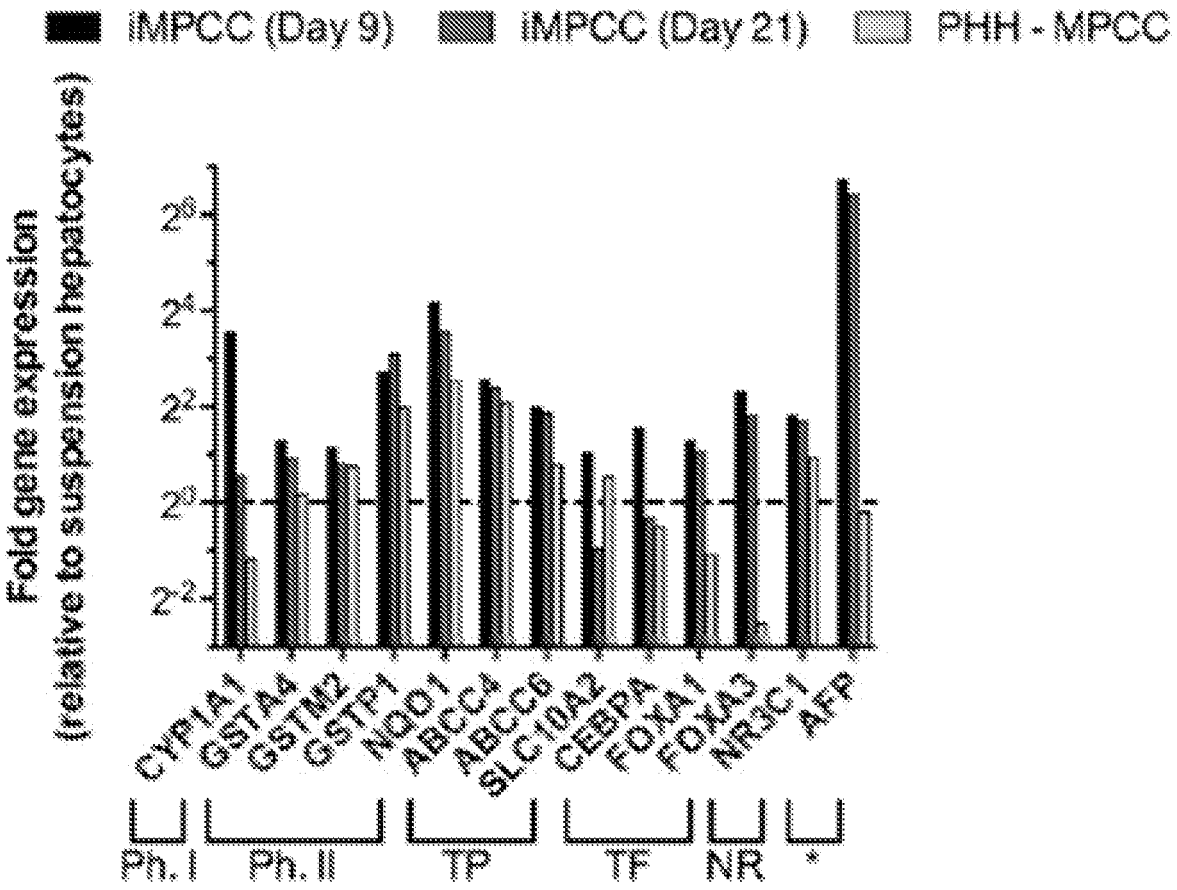
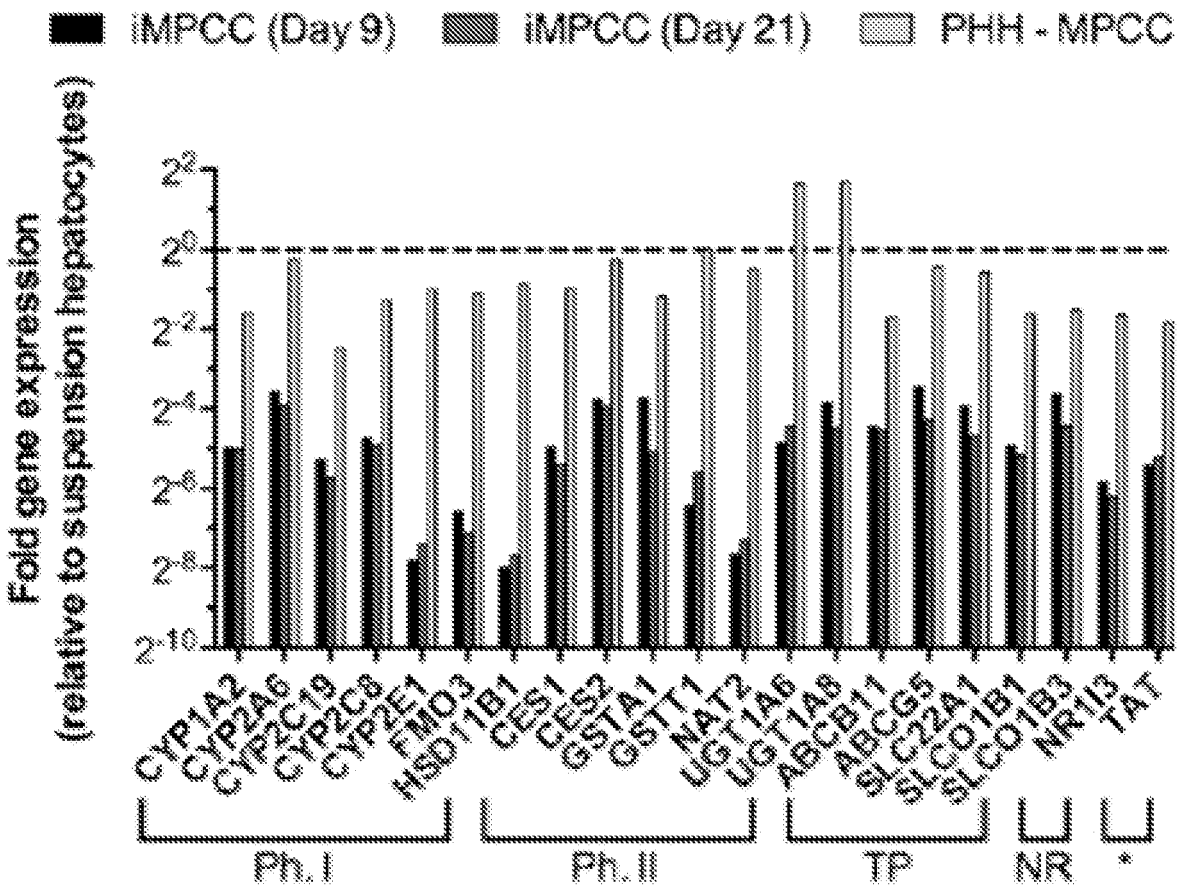


FIGURE 37A
Continued

37B



Continued
FIGURE 37B

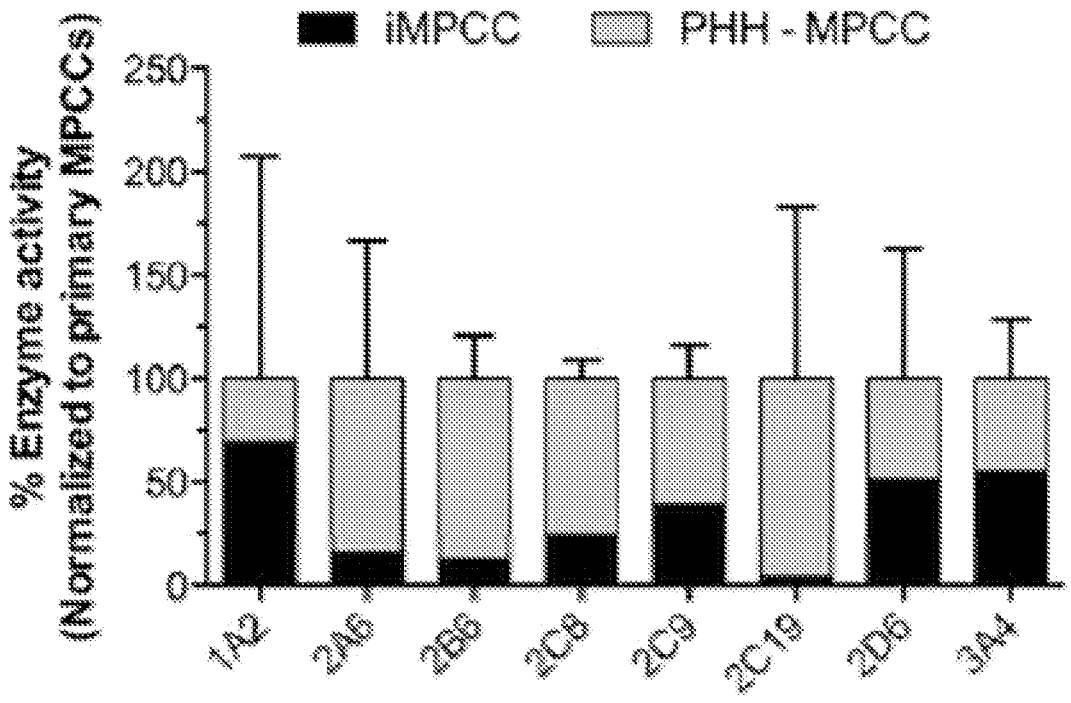

iMPCC
PHH - MPCC
% Enzyme activity
(Normalized to primary MPCCs)
250
200
150
100
50
0
1A2
2A6
2B6
2C8
2C9
2C19
2D6
3A4

FIGURE 38

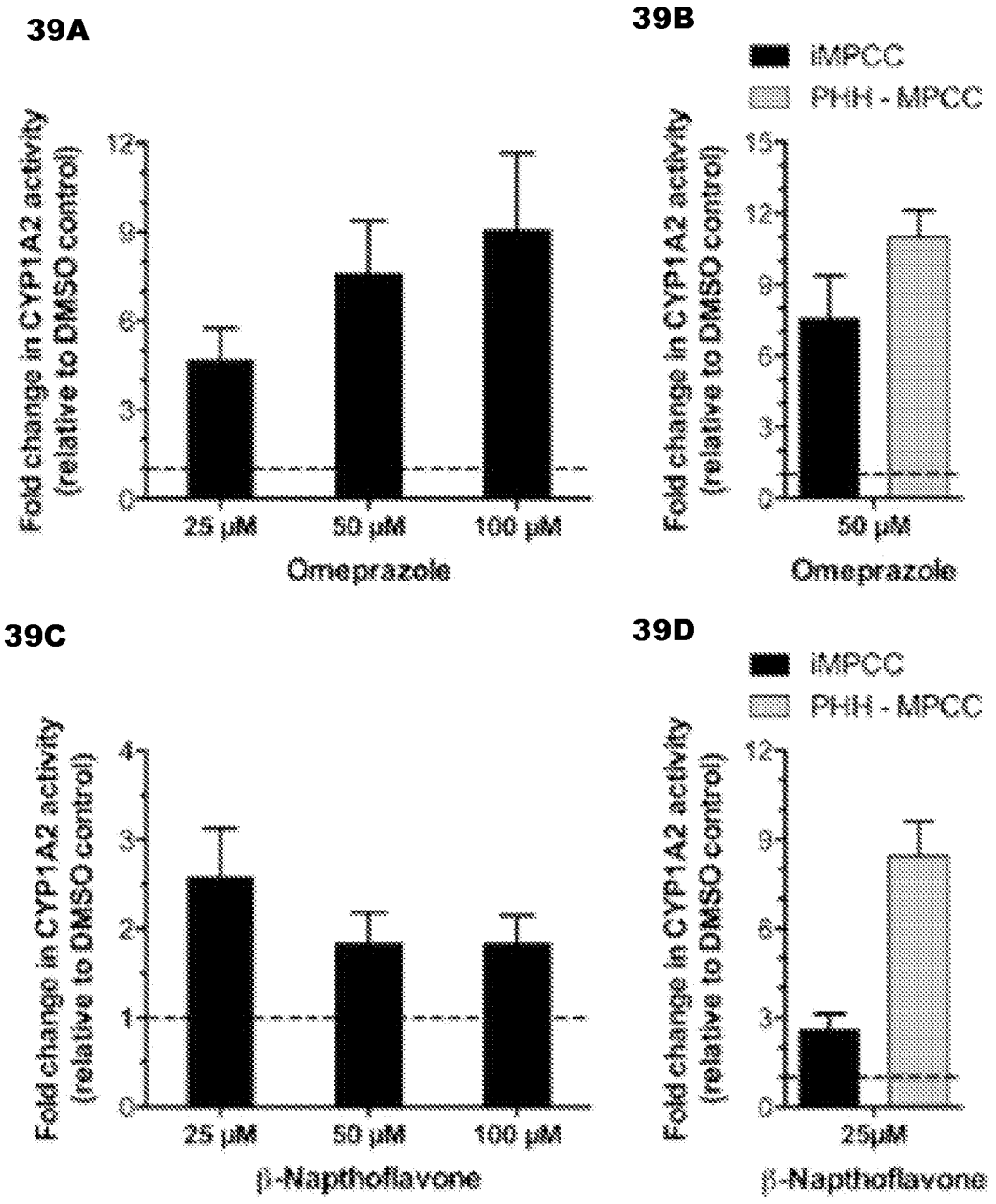


FIGURE 39A, 39B, 39C, and 39D