Fig. 1

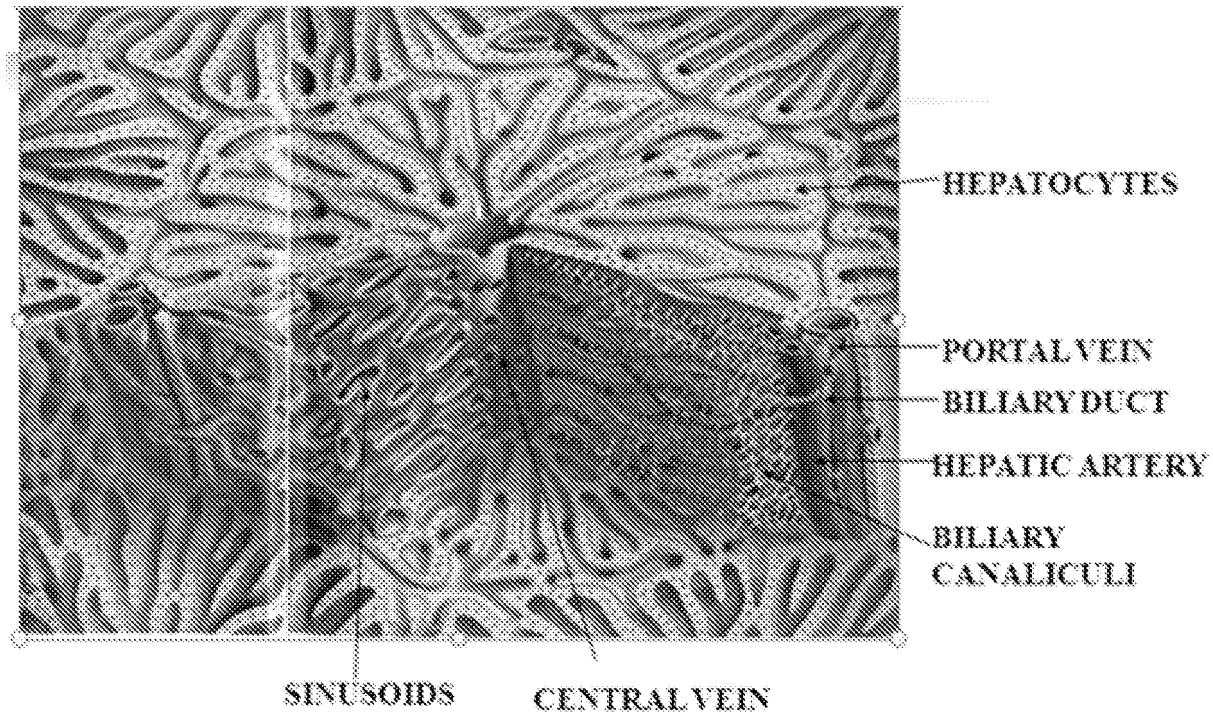

HEPATOCYTES
PORTAL VEIN
BILIARY DUCT
HEPATIC ARTERY
BILIARY CANALICULI
SINUSOIDS
CENTRAL VEIN

Fig. 2

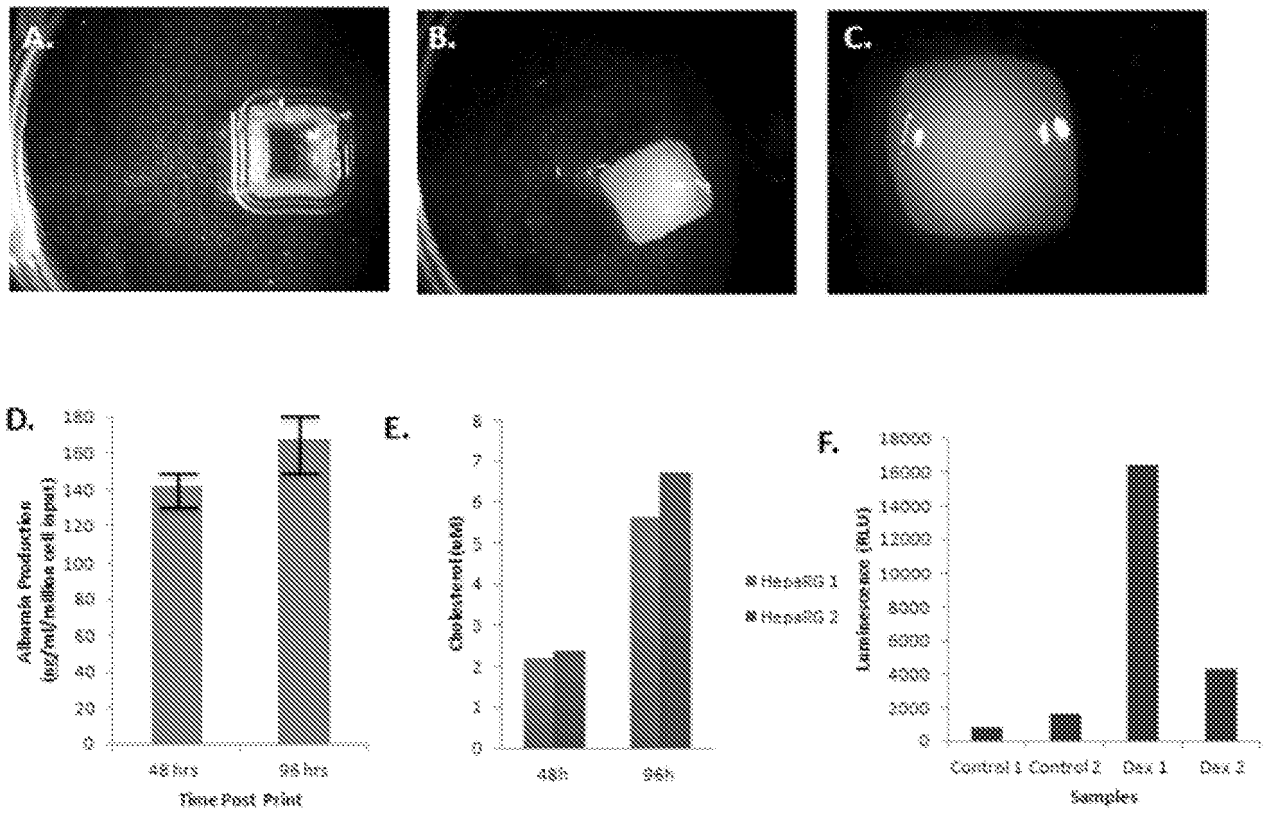
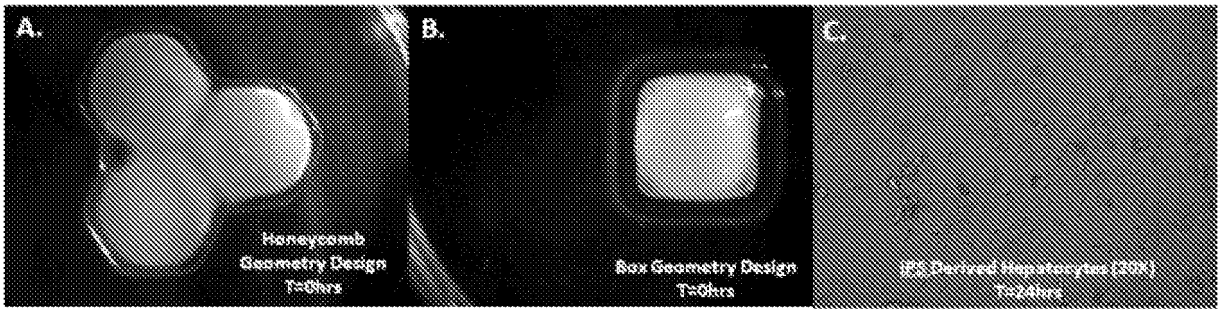

A.
B.
C.
D.
Albumin Production (ng/ml/million cell input)
48 hrs
96 hrs
Time Post Print
E.
Cholesterol (a.u.)
48h
96h
F.
HepaRG 1
HepaRG 2
Luminescence (RLU)
Control 1
Control 2
Dex 1
Dex 2
Samples

Fig. 3


A.
Honeycomb
Geometry Design
T=0hrs
B.
Box Geometry Design
T=0hrs
C.

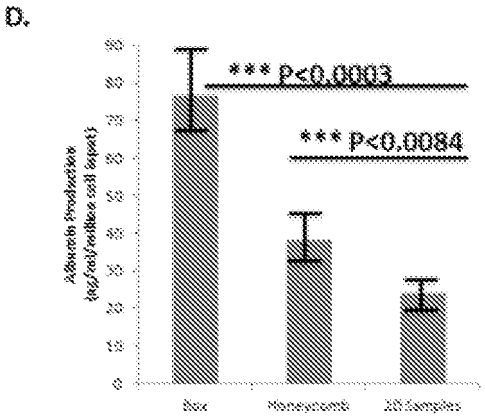

D.
*** P<0.0003
*** P<0.0084

Fig. 4

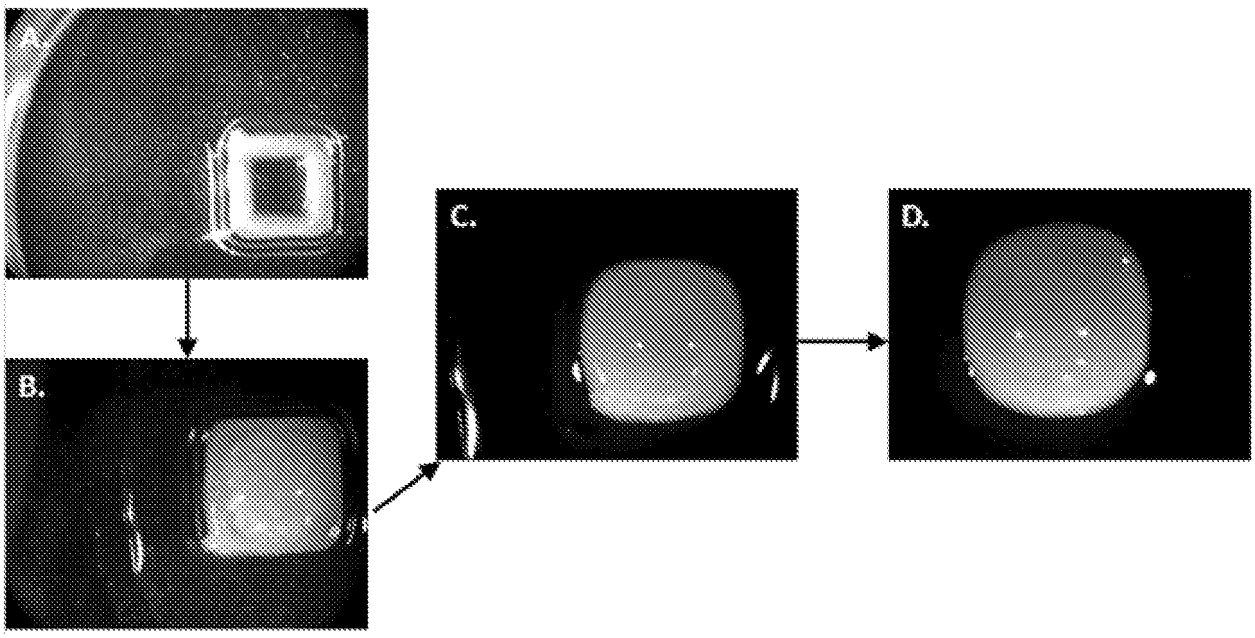


Fig. 5

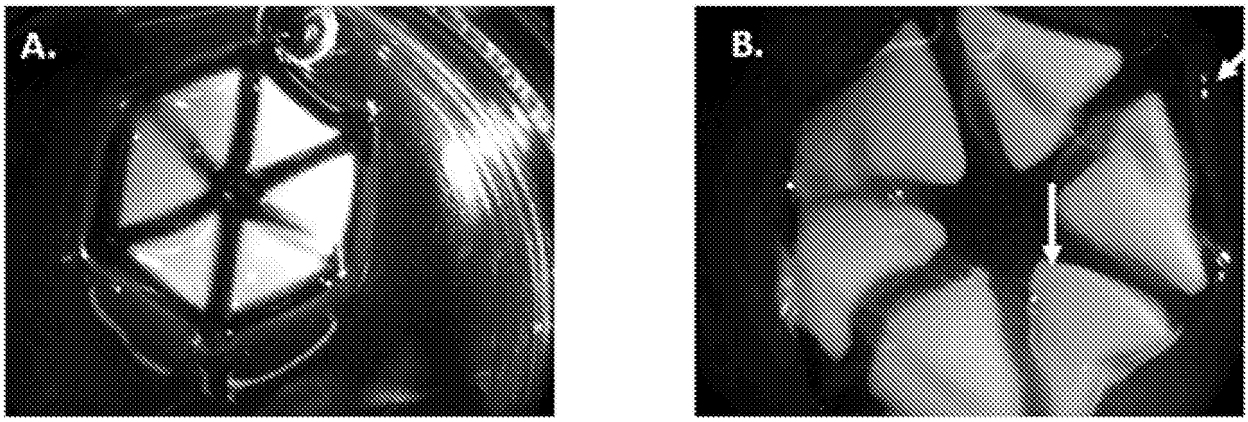


Fig. 6

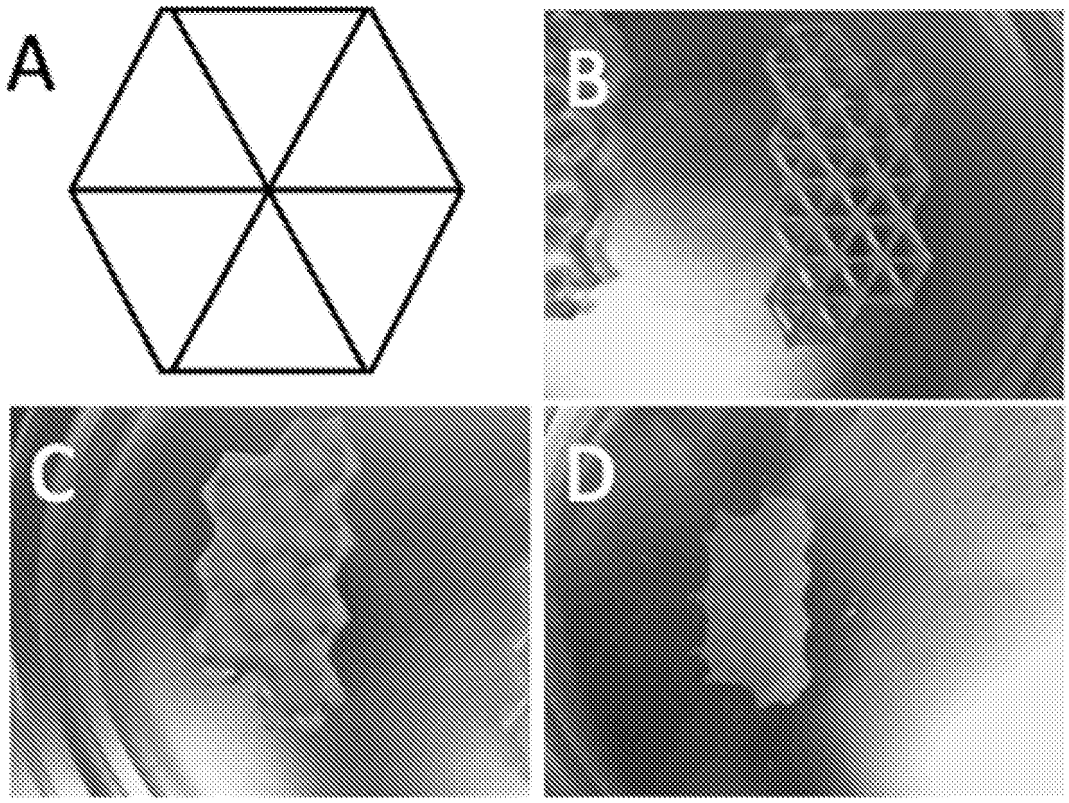


Fig. 7

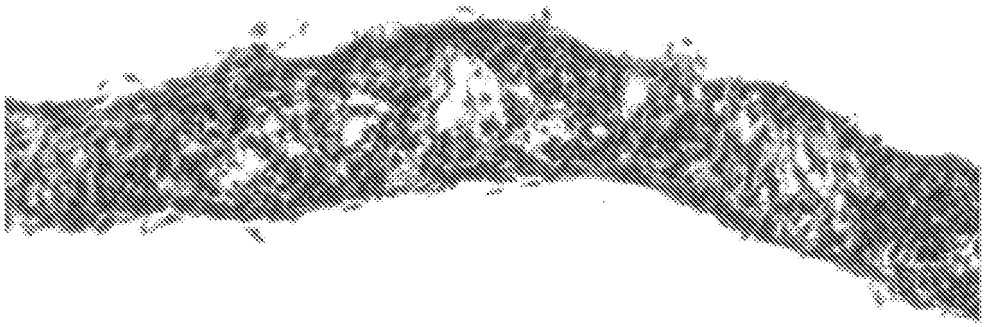


Fig. 8

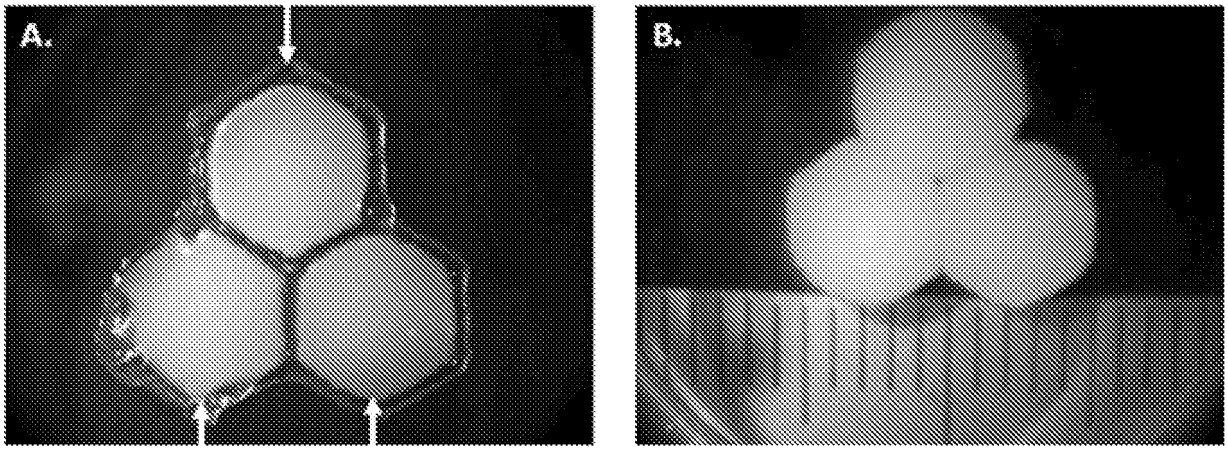


Fig. 9

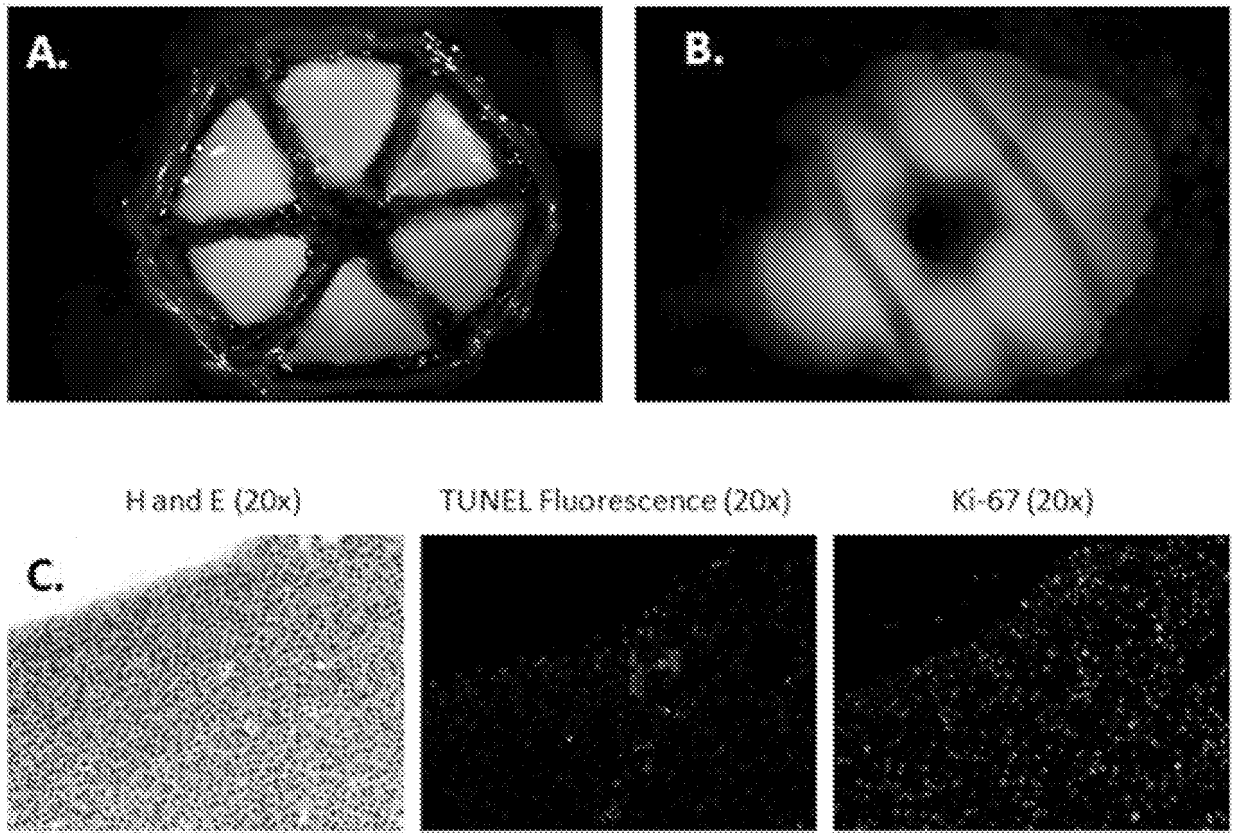


Fig. 10

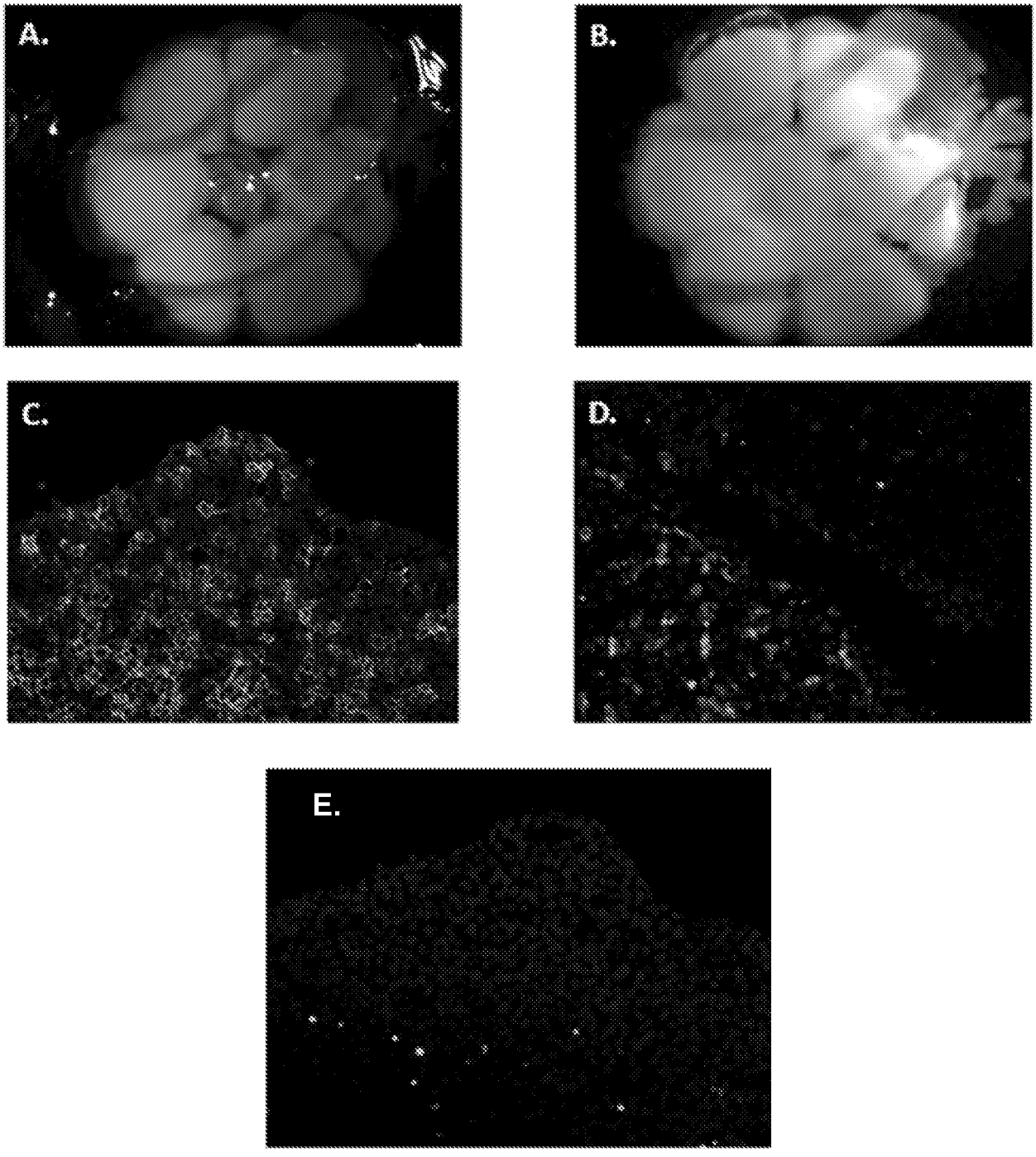


Fig. 11

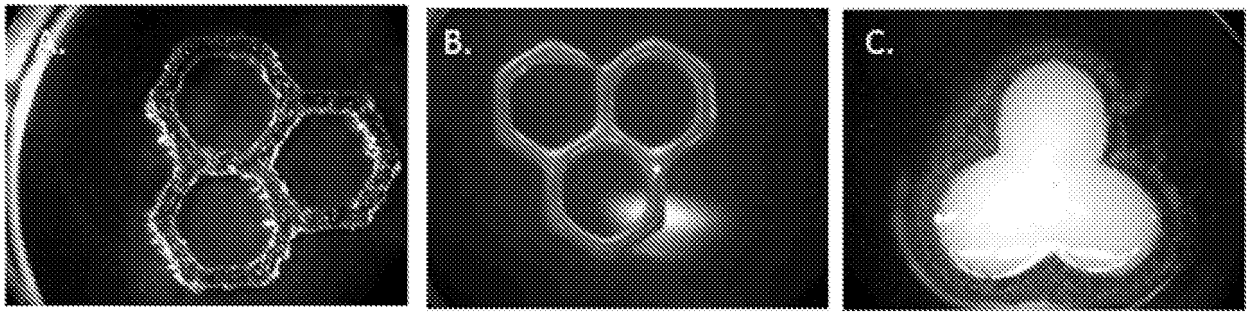


Fig. 12

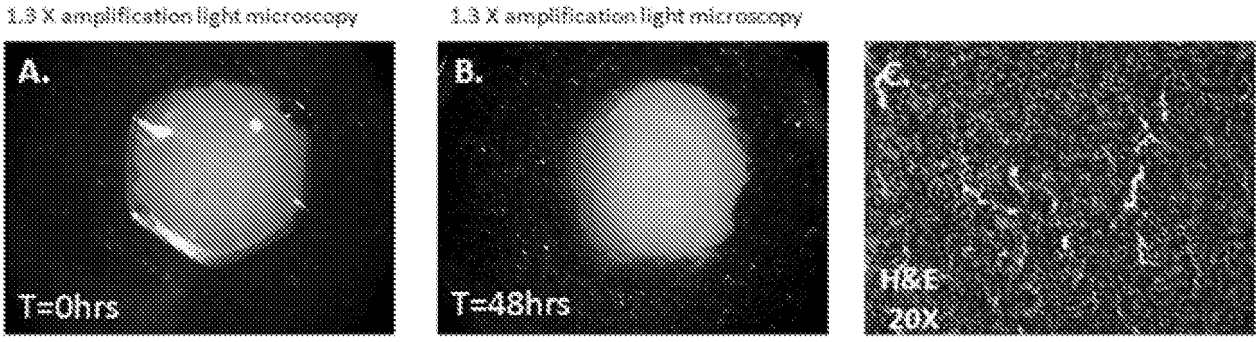

1.3 X amplification light microscopy
A.
T=0hrs
1.3 X amplification light microscopy
B.
T=48hrs
C.
H&E
20X

Fig. 13

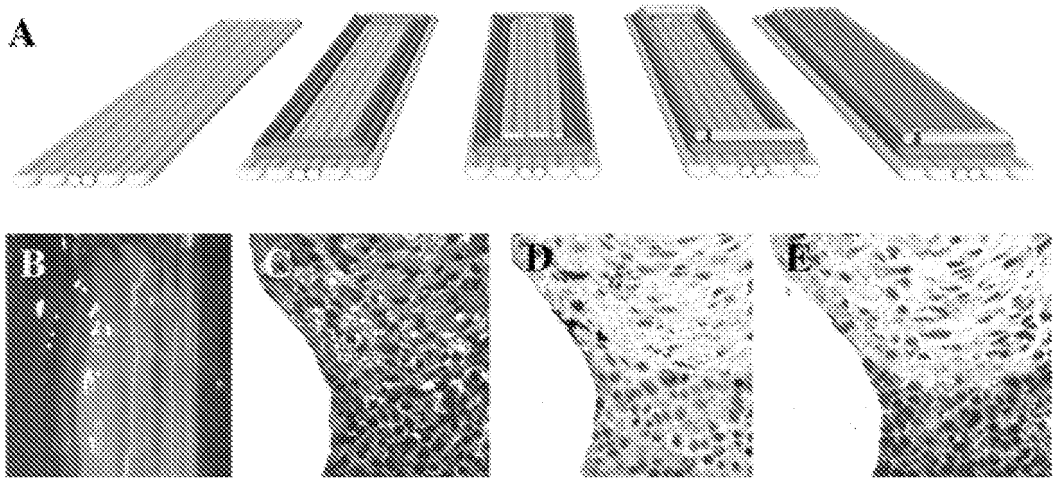


Fig. 14

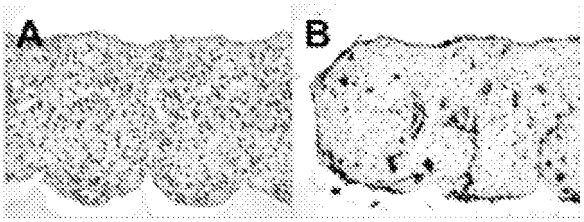


Fig. 15

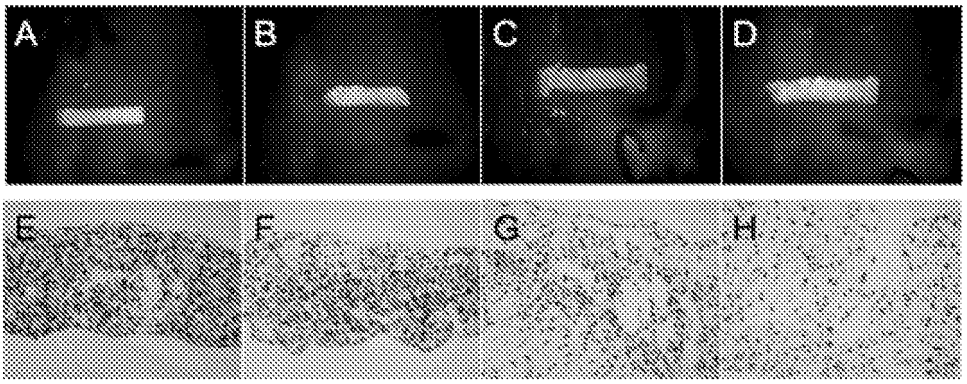


Fig. 16

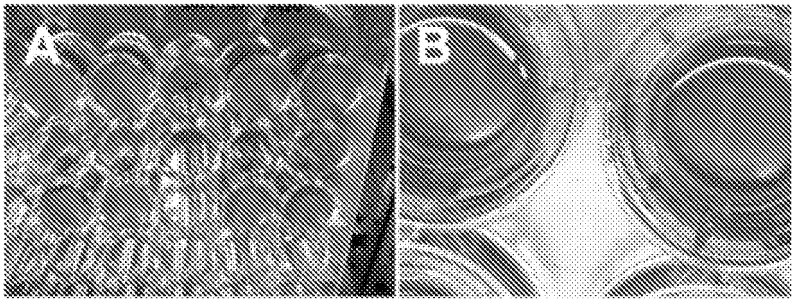


Fig. 17

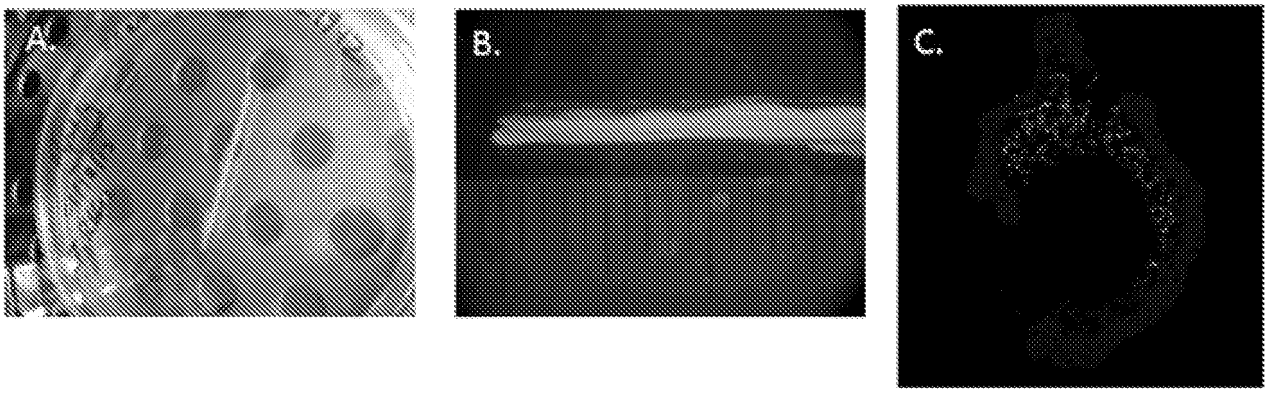


Fig. 18

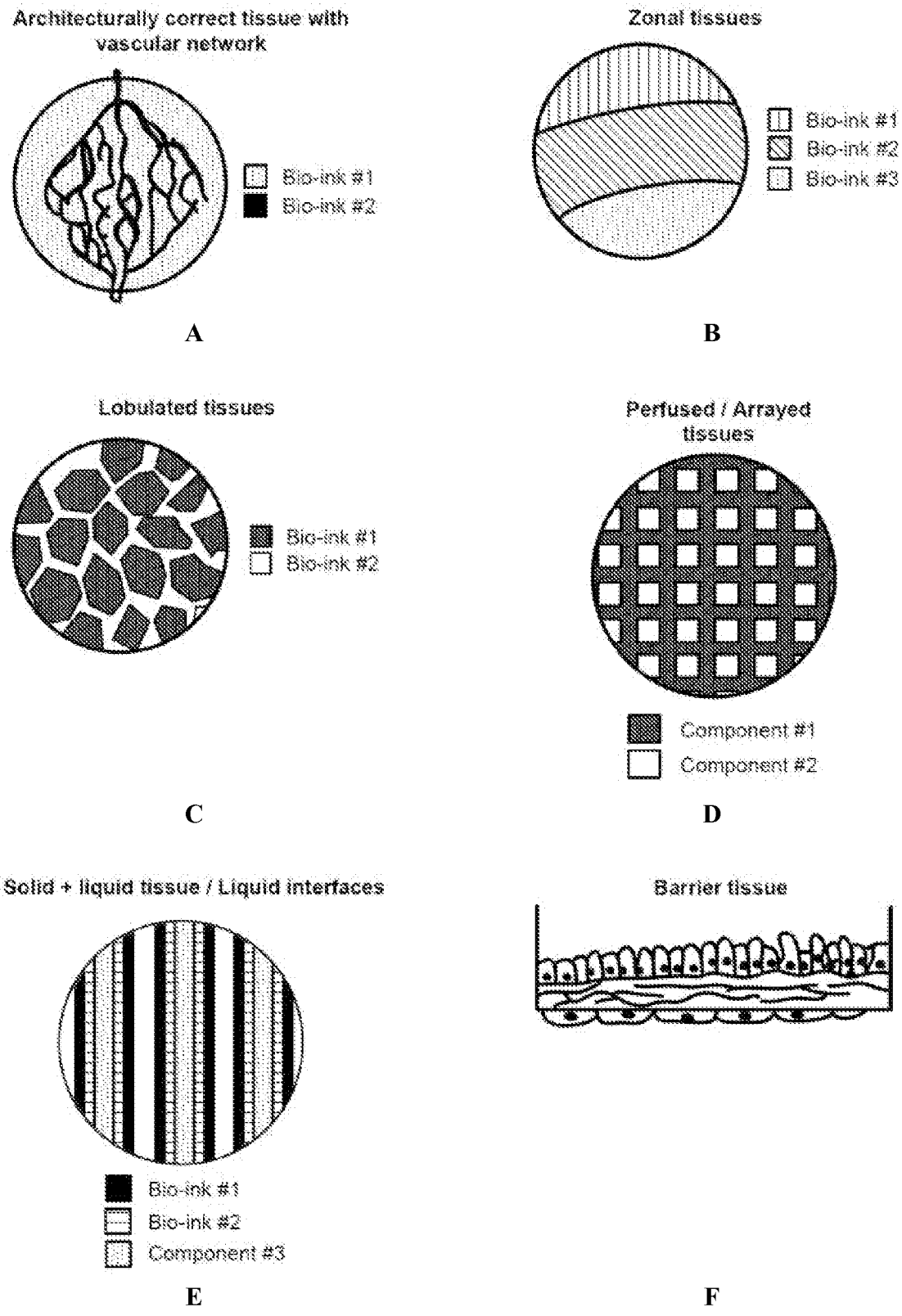
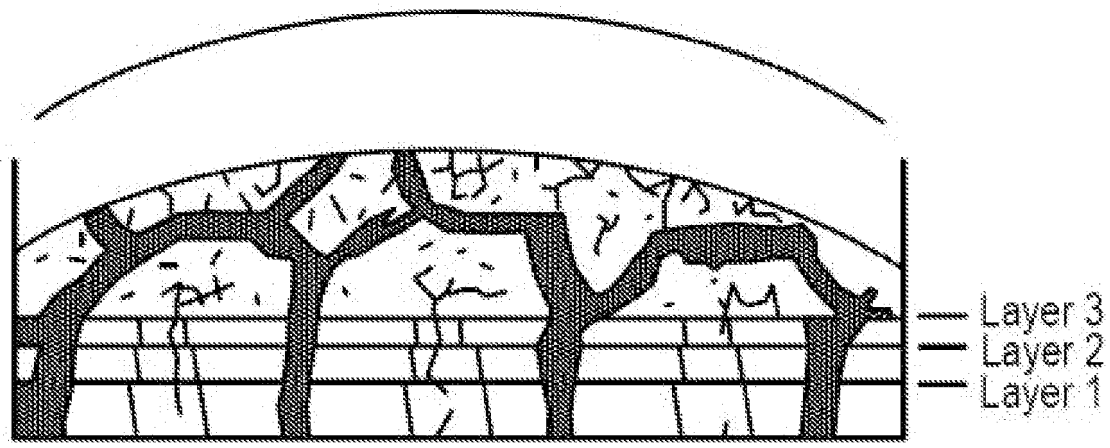

Architecturally correct tissue with vascular network
Bio-ink #1
Bio-ink #2
A
Zonal tissues
Bio-ink #1
Bio-ink #2
Bio-ink #3
B
Lobulated tissues
Bio-ink #1
Bio-ink #2
C
Perfused / Arrayed tissues
Component #1
Component #2
D
Solid + liquid tissue / Liquid interfaces
Bio-ink #1
Bio-ink #2
Component #3
E
Barrier tissue
F

Fig. 18 (cont.)



G

Fig. 19

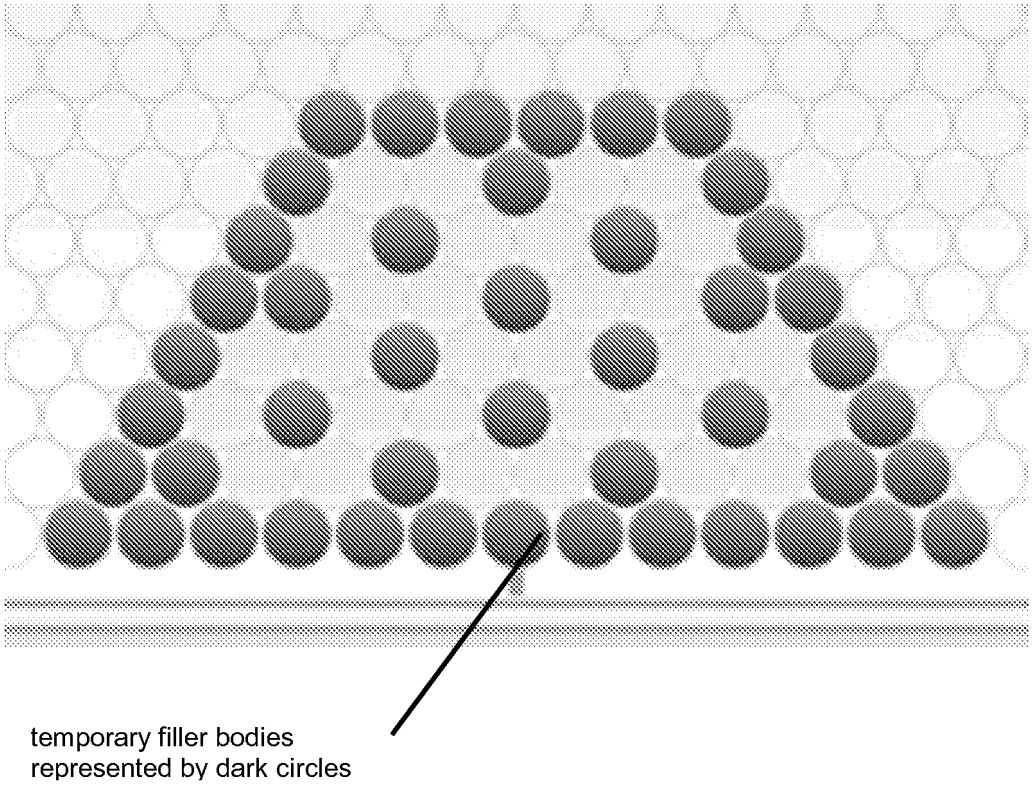


Fig. 20

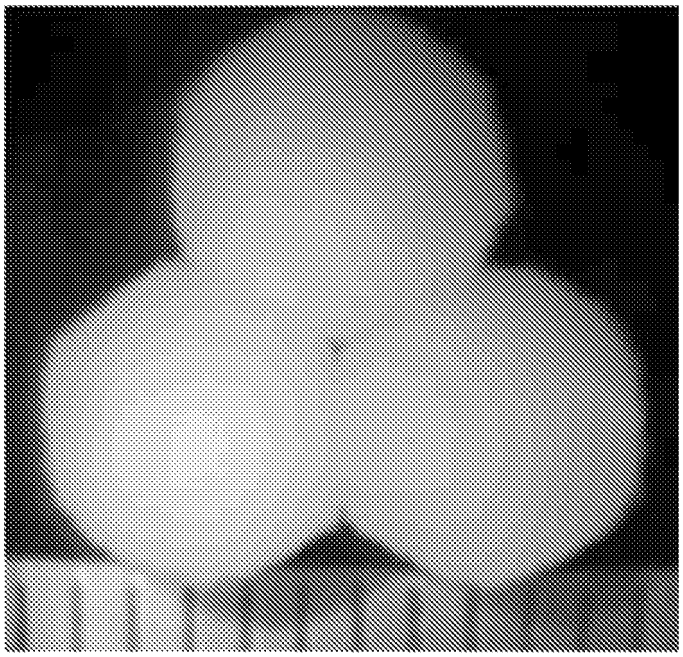


Fig. 21

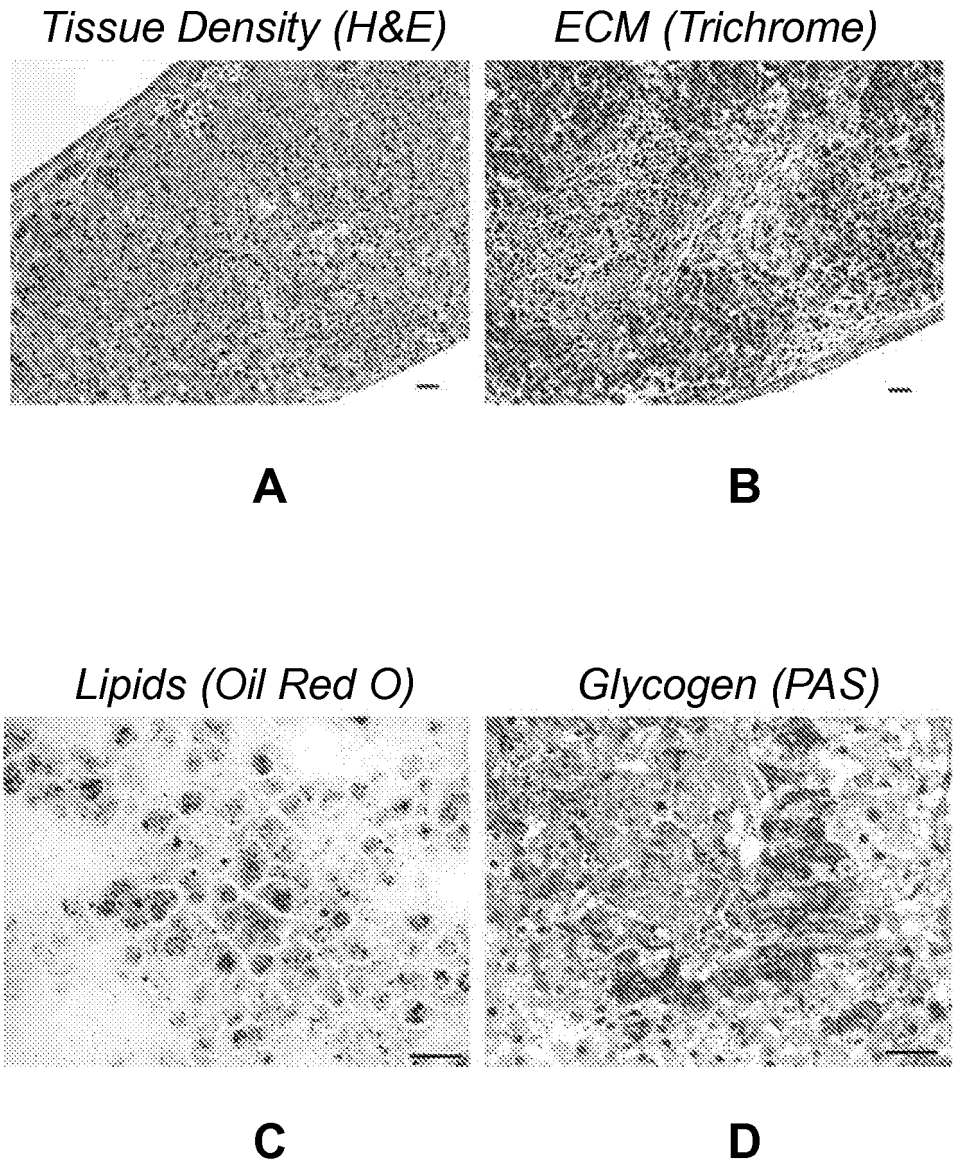

Tissue Density (H&E)
ECM (Trichrome)
A
B
Lipids (Oil Red O)
Glycogen (PAS)
C
D

Fig. 22

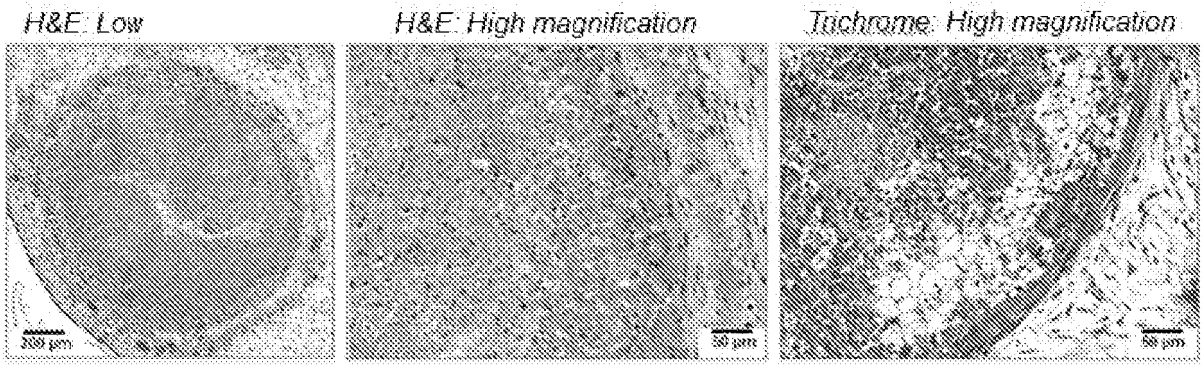

H&E: Low
H&E: High magnification
Trichrome: High magnification
A
C
B

Fig. 23

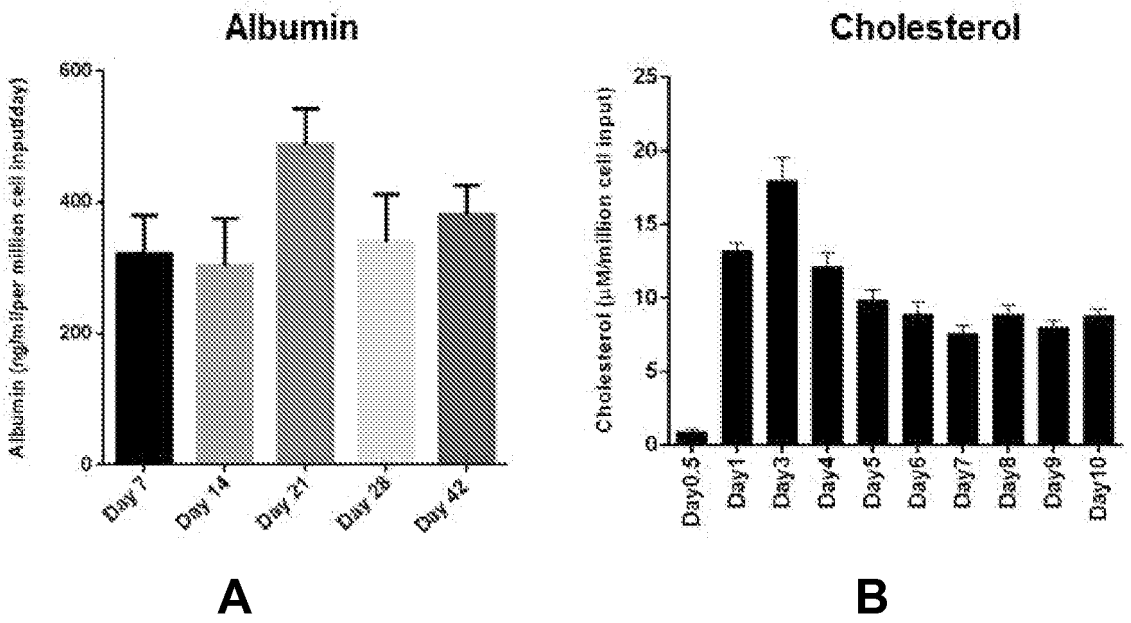
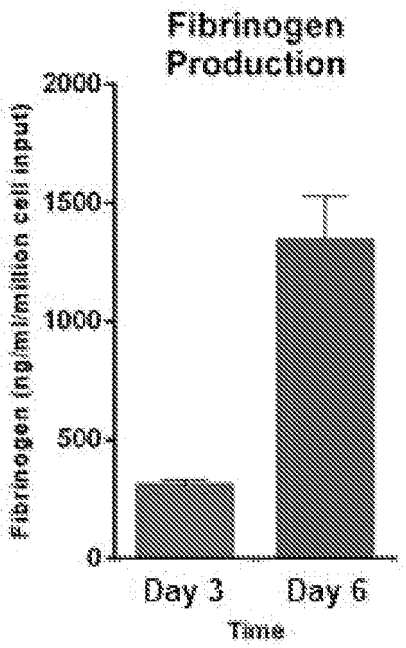
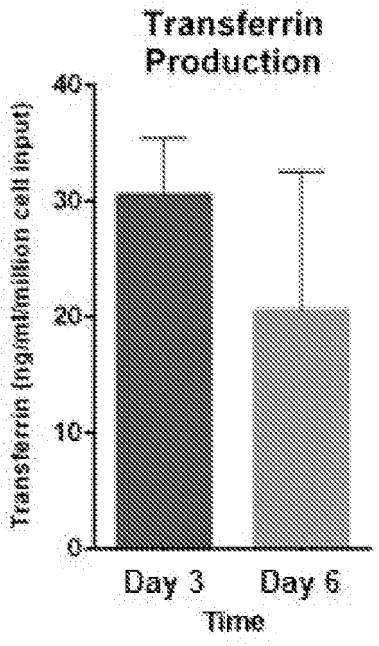

Albumin
Albumin (ng/ml/per million cell input/day)
600
400
200
0
Day 7
Day 14
Day 21
Day 28
Day 42
A
Cholesterol
Cholesterol (μM/million cell input)
25
20
15
10
5
0
Day0.5
Day1
Day3
Day4
Day5
Day6
Day7
Day8
Day9
Day10
B

Fig. 24


Fibrinogen Production
Fibrinogen (ng/million cell input)
2000
1500
1000
500
0
Day 3
Day 6
Time

A


Transferrin Production
Transferrin (ng/million cell input)
40
30
20
10
0
Day 3
Day 6
Time

B

Fig. 25

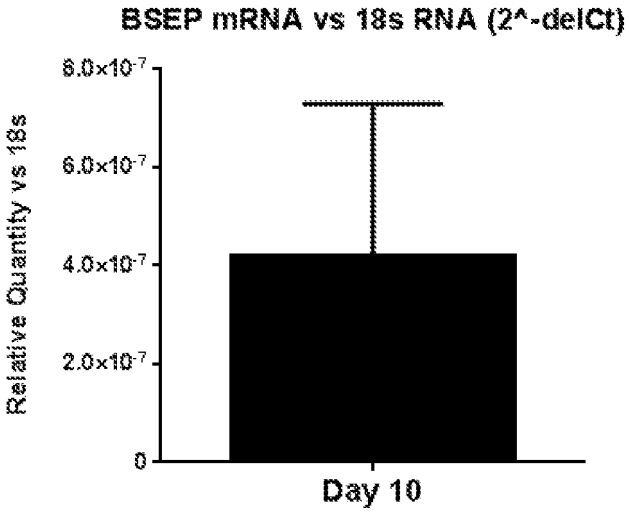
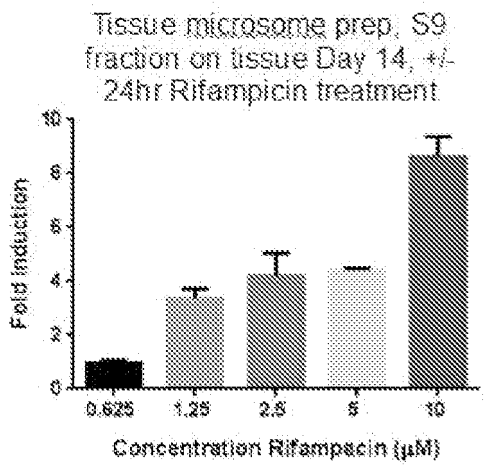
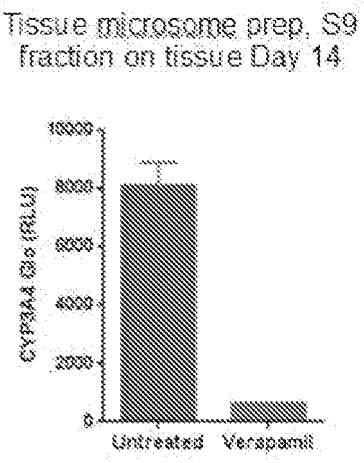

BSEP mRNA vs 18s RNA (2^-delCt)
Relative Quantity vs 18s
8.0x10-7
6.0x10-7
4.0x10-7
2.0x10-7
0
Day 10

Fig. 26


Tissue microsome prep, S9 fraction on tissue Day 14, +/- 24hr Rifampicin treatment
Fold Induction
0
2
4
6
8
10
0.625
1.25
2.5
5
10
Concentration Rifampacin (µM)

A


Tissue microsome prep, S9 fraction on tissue Day 14
CYP3A4 (Bfc (RLU)
0
2000
4000
6000
8000
10000
Untreated
Verapamil

B

Fig. 27

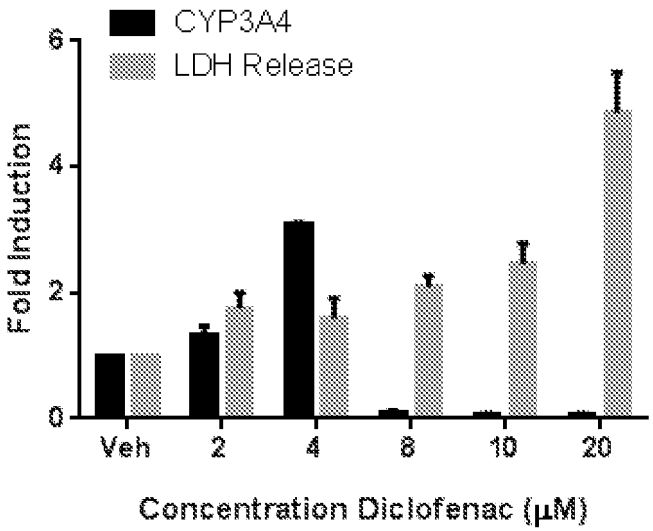
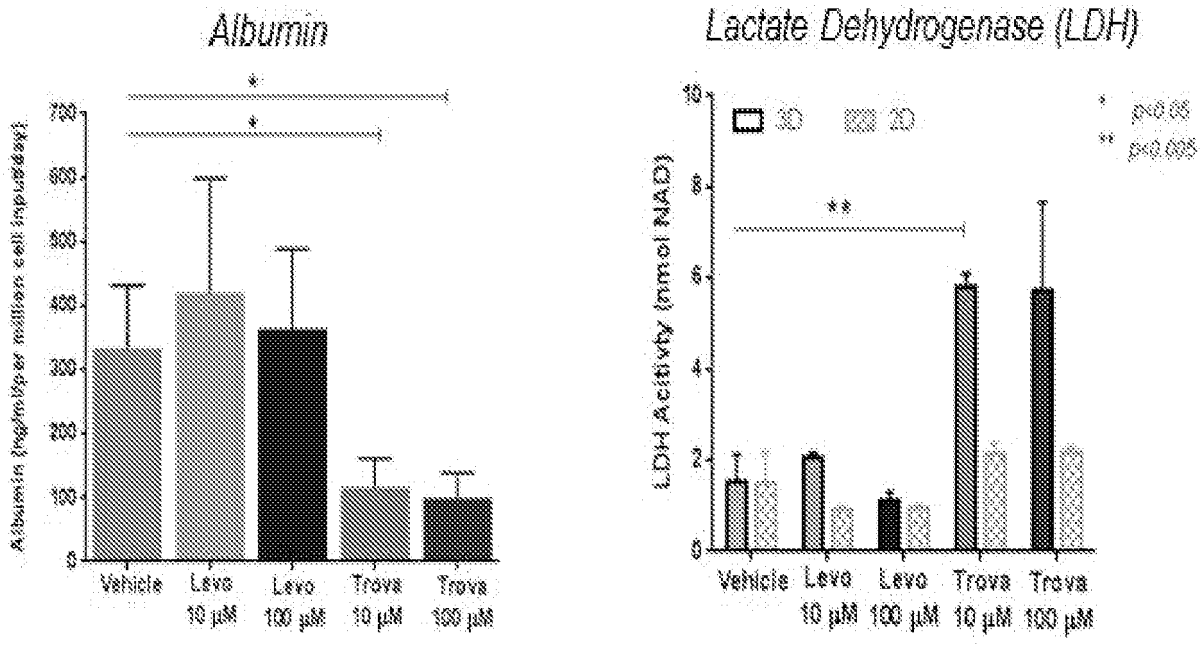

CYP3A4
LDH Release
Fold Induction
0
2
4
6
Veh
2
4
8
10
20
Concentration Diclofenac (μM)

Fig. 28


Albumin
Albumin (ng/ml/per million cell input/day)
Vehicle
Levo 10 µM
Levo 100 µM
Trova 10 µM
Trova 100 µM
Lactate Dehydrogenase (LDH)
LDH Activity (nmol NAD)
3D
2D
* p<0.05
** p<0.005

A B

Fig. 29

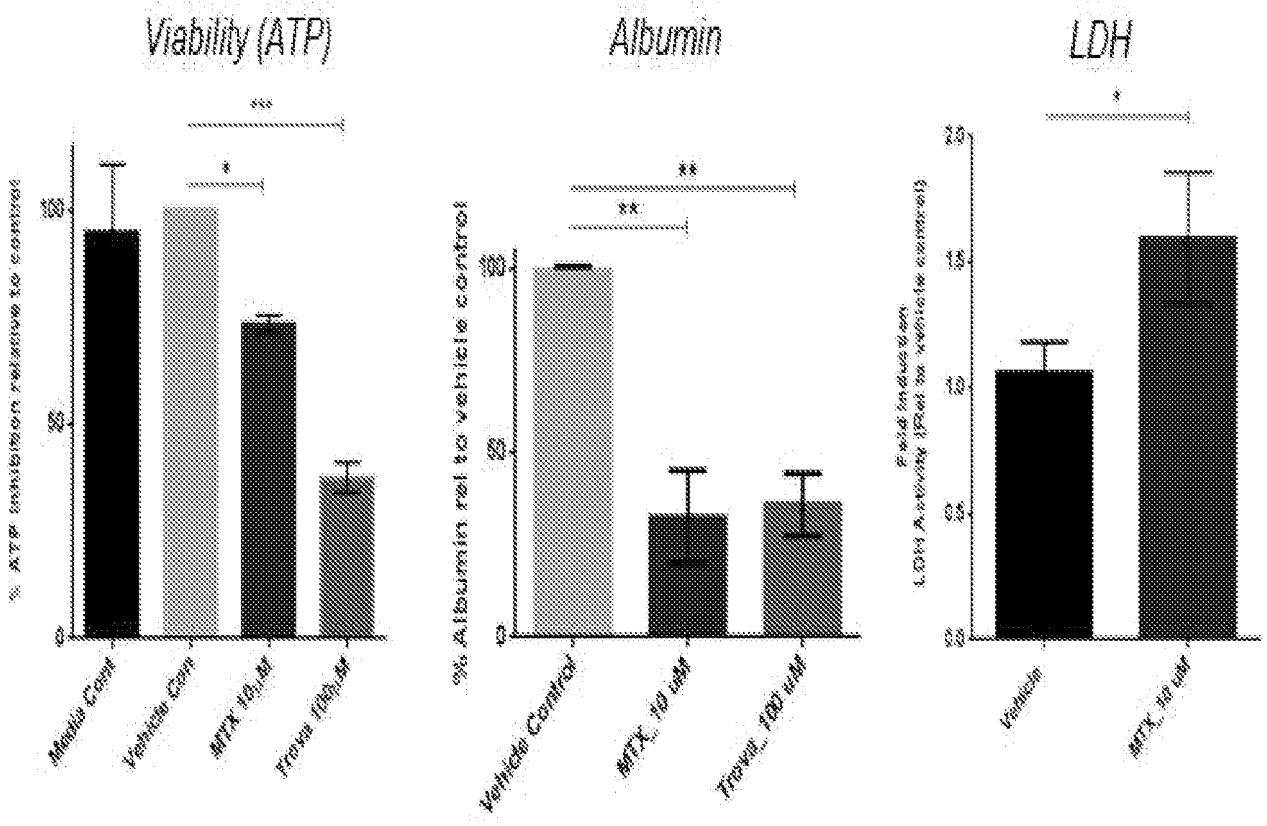

Viability (ATP)
Albumin
LDH
Media Cont
Vehicle Cont
MTX, 10 uM
Trovar, 100 uM
Vehicle Control
Vehicle
A
B
C

Fig. 30

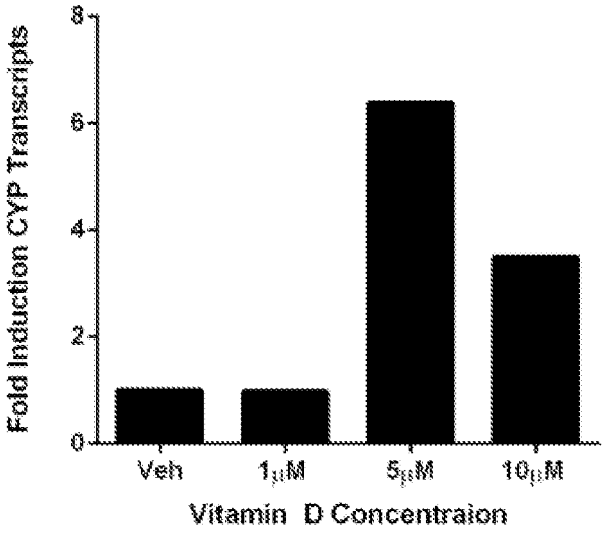

Fold Induction CYP Transcripts
8
6
4
2
0
Veh
1μM
5μM
10μM
Vitamin D Concentraion

Fig. 31

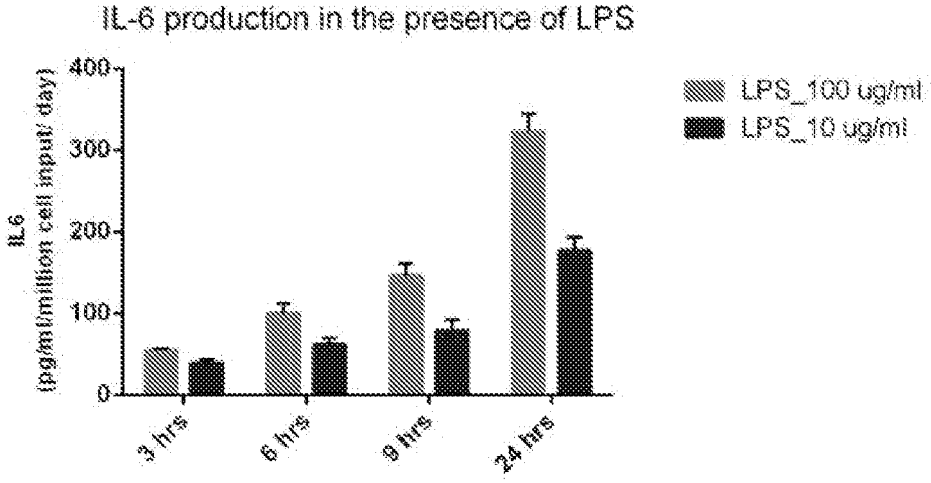

IL-6 production in the presence of LPS
IL6 (pg/ml/million cell input/ day)
400
300
200
100
0
3 hrs
6 hrs
9 hrs
24 hrs
LPS_100 ug/ml
LPS_10 ug/ml

Fig. 32a

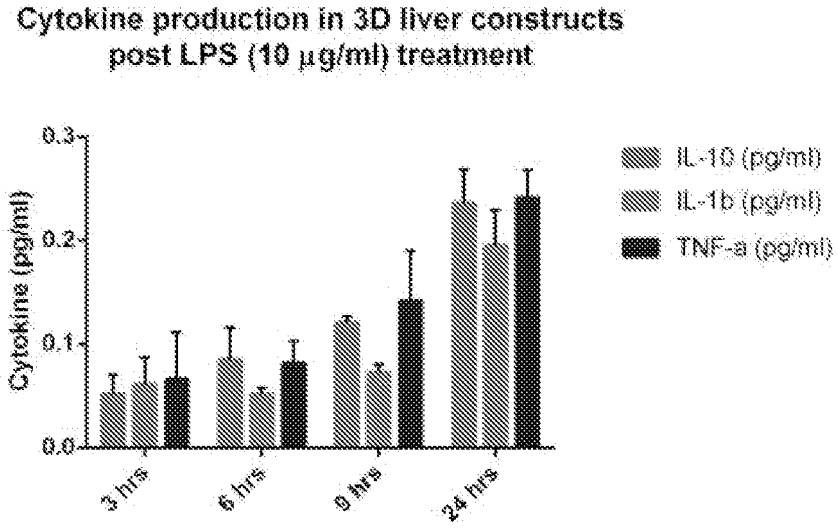


Fig. 32b

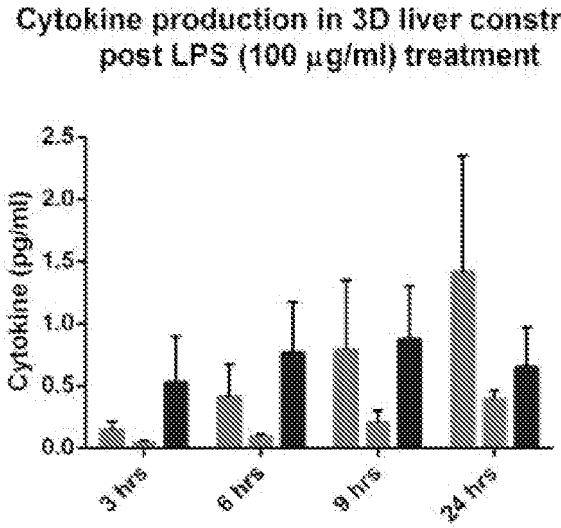


Fig. 33

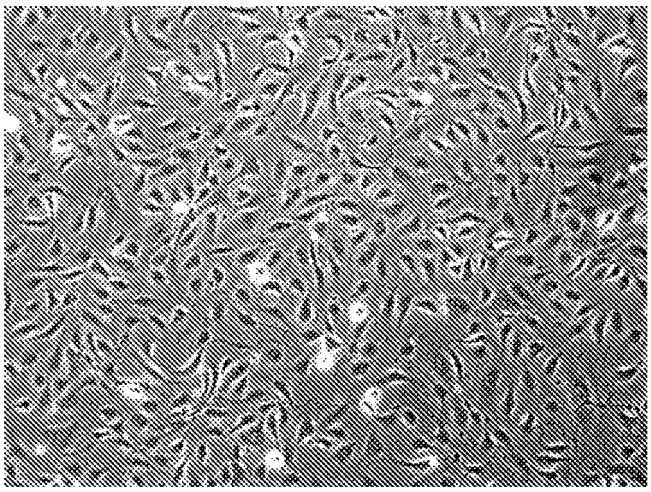


Fig. 34

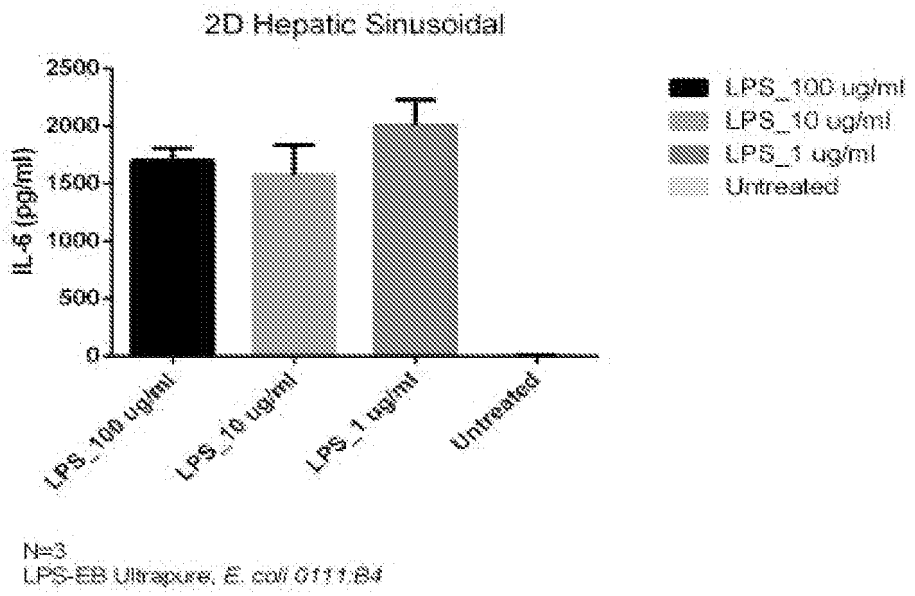

2D Hepatic Sinusoidal
IL-6 (pg/ml)
2500
2000
1500
1000
500
0
LPS_100 ug/ml
LPS_10 ug/ml
LPS_1 ug/ml
Untreated
N=3
LPS-EB Ultrapure, E. coli 0111:B4

Fig. 35

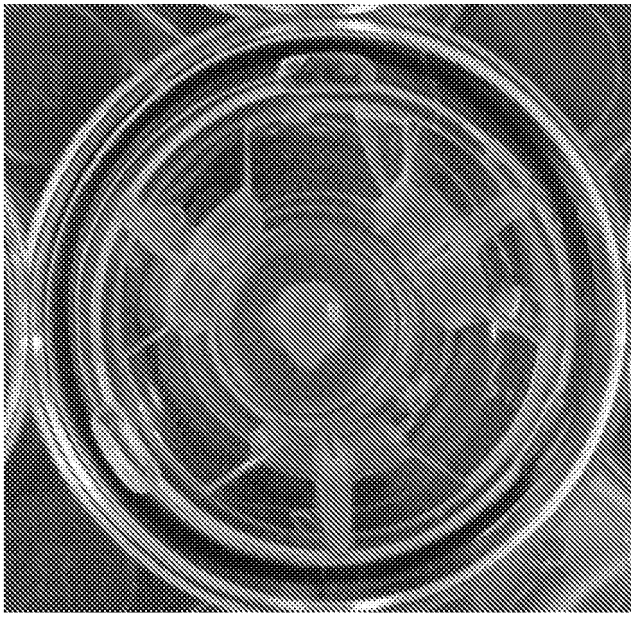


Fig. 36

