Figure 1

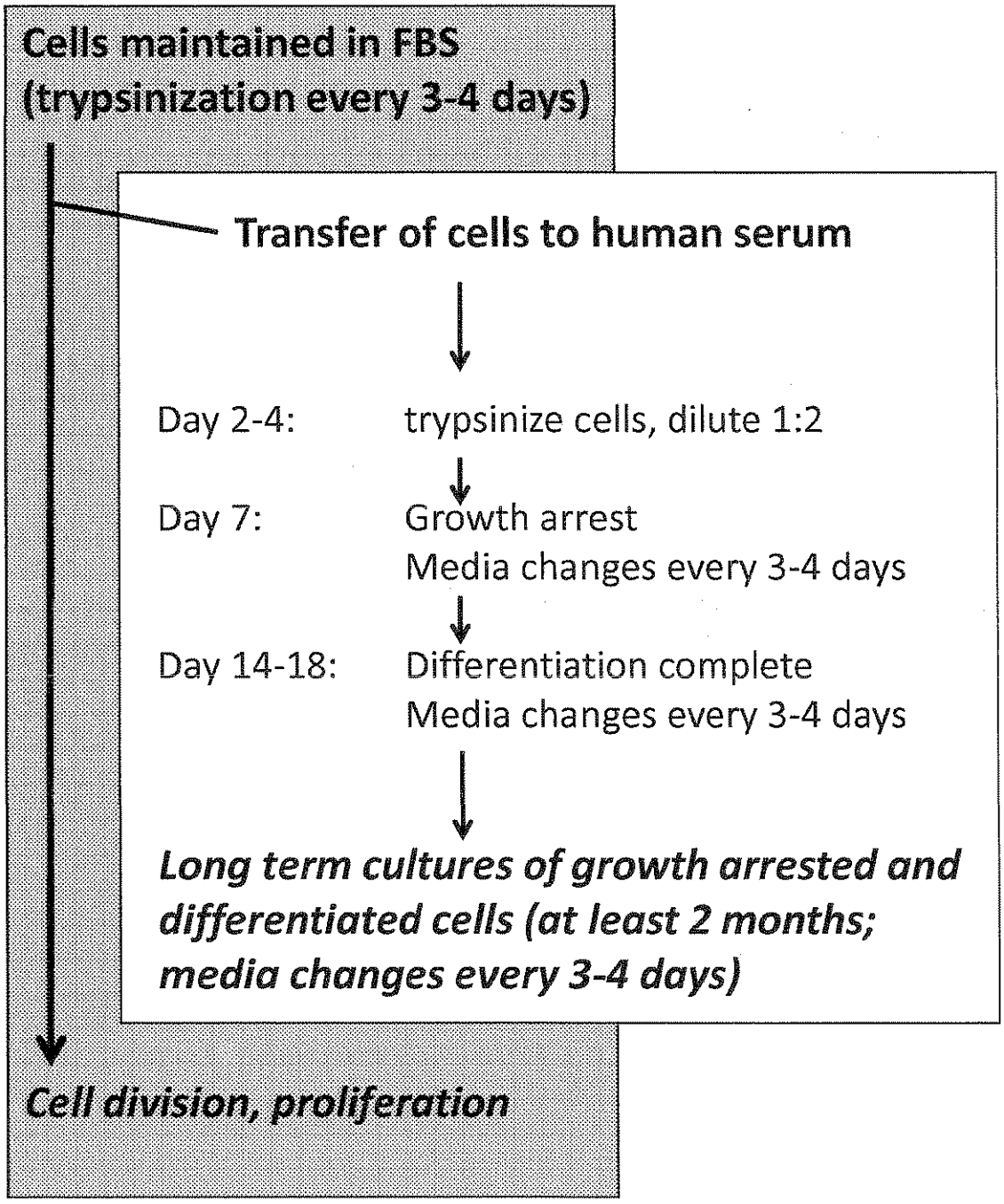
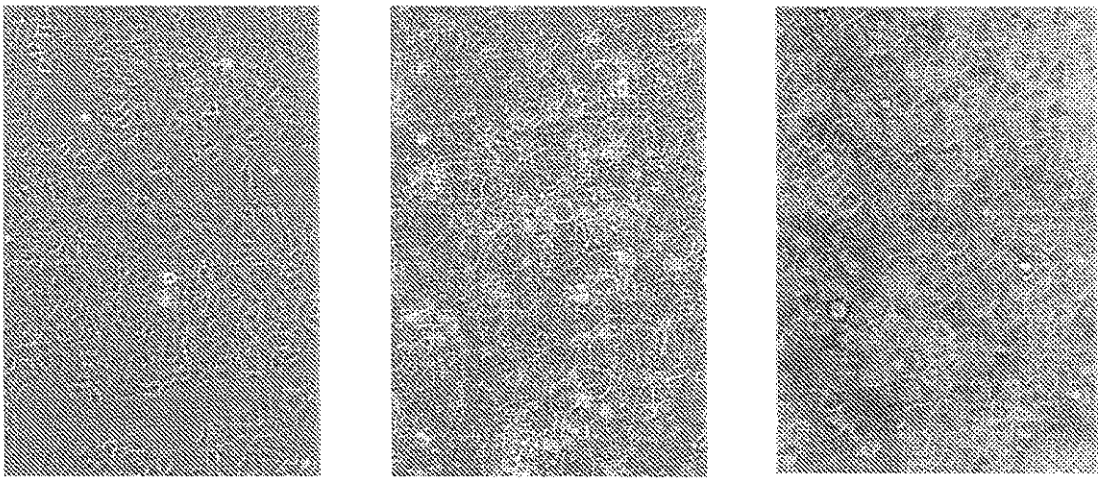

Cells maintained in FBS
(trypsinization every 3-4 days)
Transfer of cells to human serum
Day 2-4:
trypsinize cells, dilute 1:2
Day 7:
Growth arrest
Media changes every 3-4 days
Day 14-18:
Differentiation complete
Media changes every 3-4 days
Long term cultures of growth arrested and differentiated cells (at least 2 months; media changes every 3-4 days)
Cell division, proliferation

Figure 2A



Huh7.5 cells grown in FBS containing medium

Huh7.5 cells maintained in HS containing medium for 21 days

Human primary hepatocytes grown on collagen coated dishes

Figure 2B

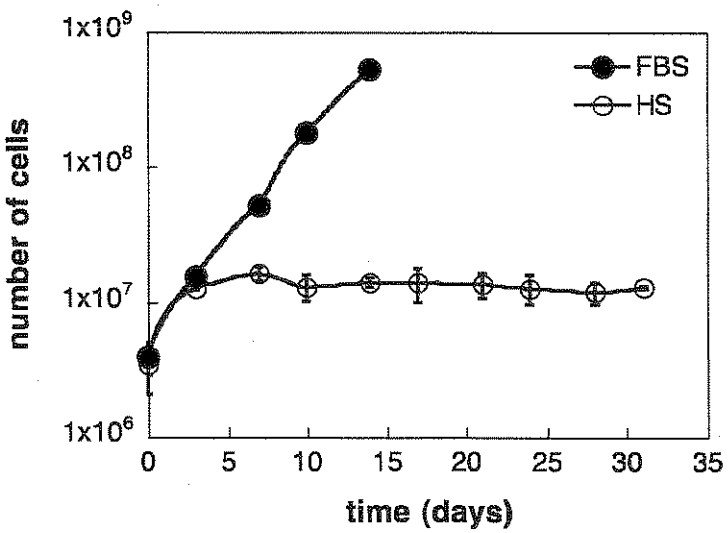


Figure 3A

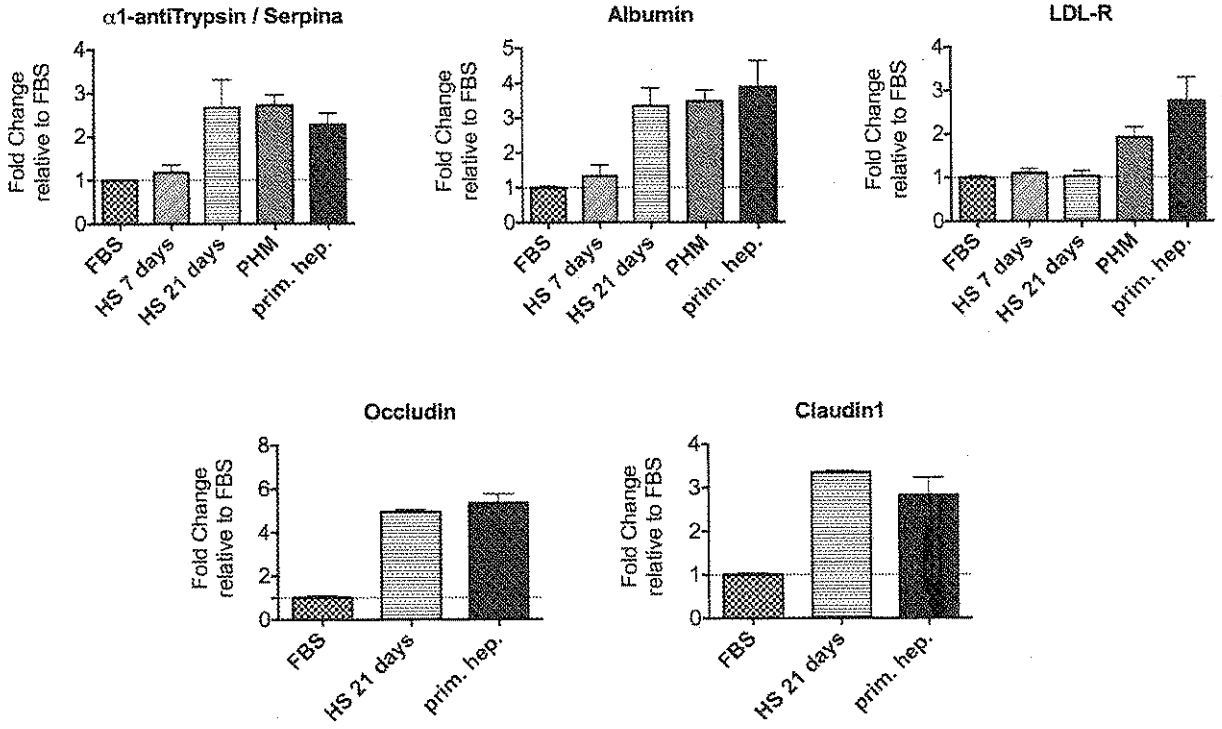


Figure 3B

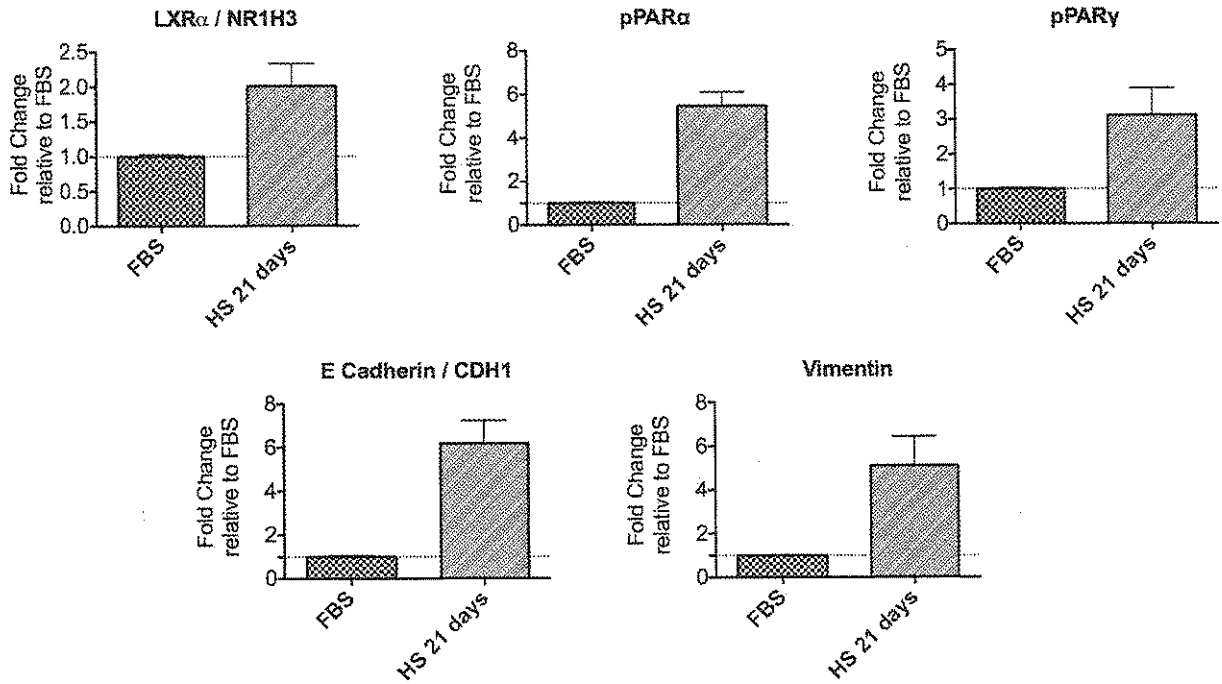


Figure 4

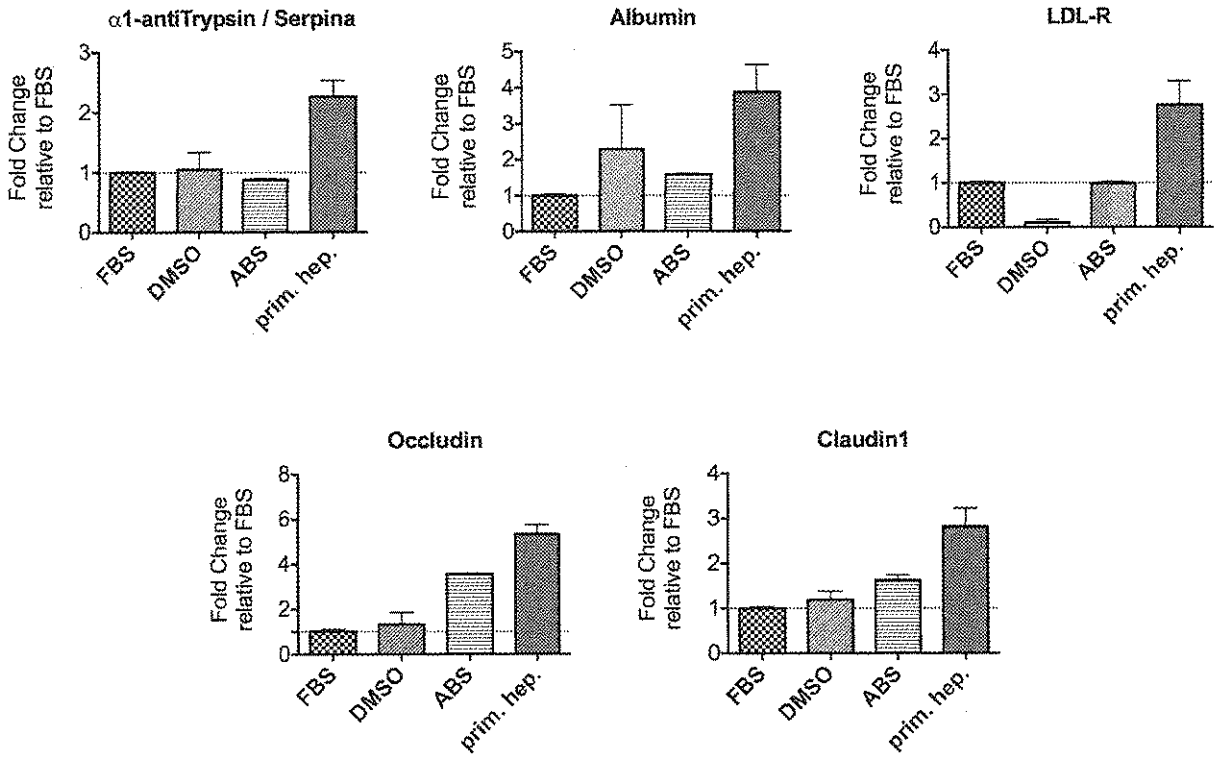

α1-antiTrypsin / Serpina
Albumin
LDL-R
Occludin
Claudin1
Fold Change relative to FBS
FBS
DMSO
ABS
prim. hep.

Figure 5A

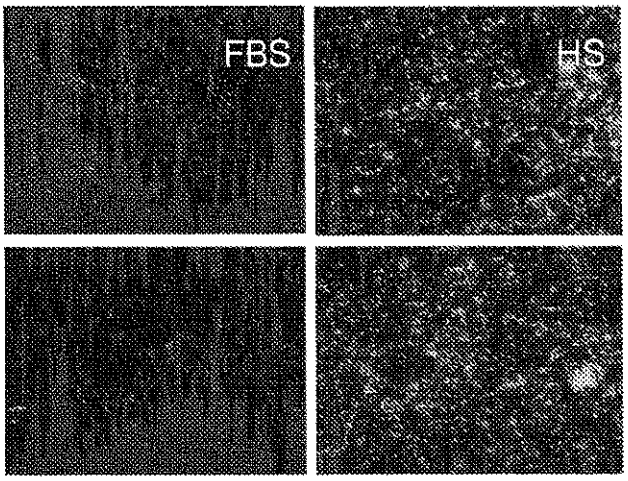


Figure 5B

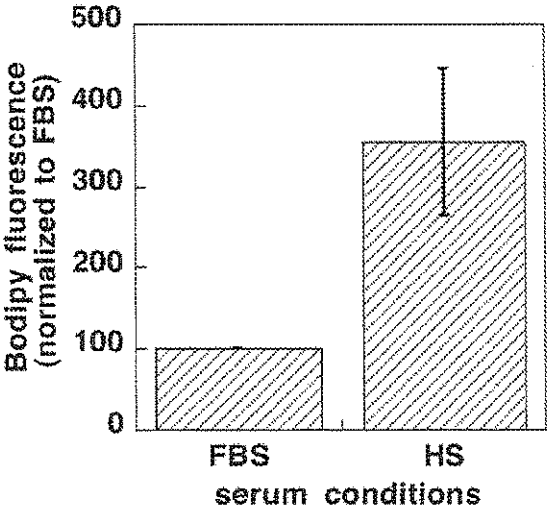


Figure 6A

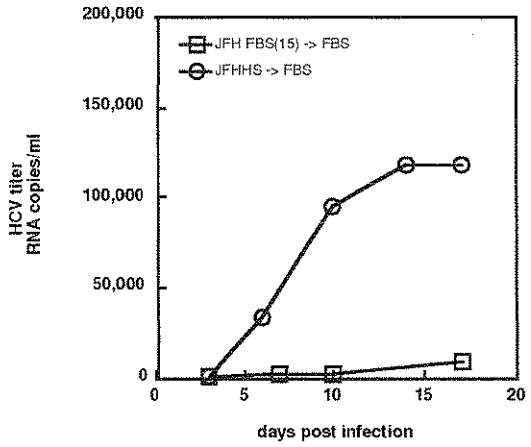


Figure 6B

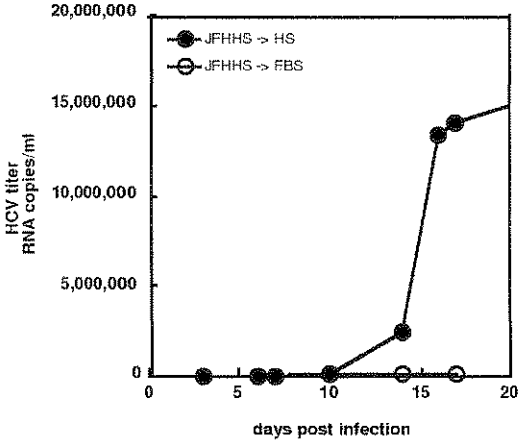


Figure 6C

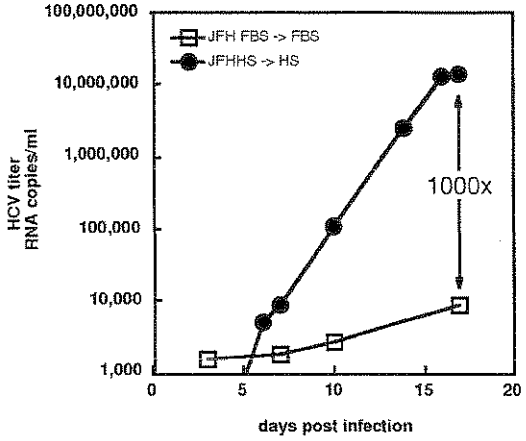


Figure 6

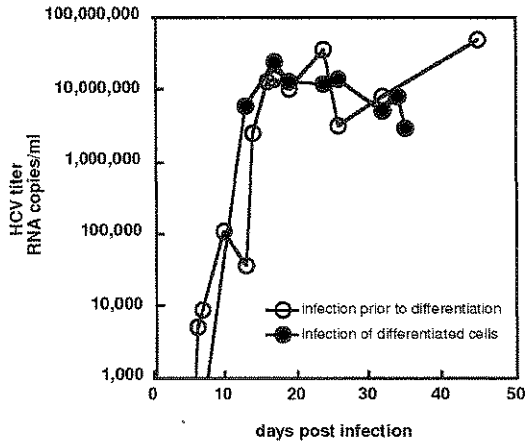


Figure 6E

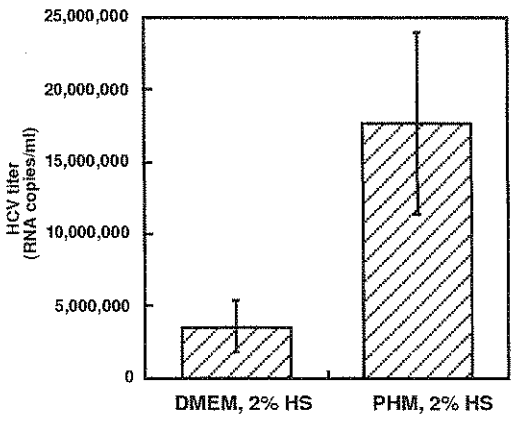


Figure 7

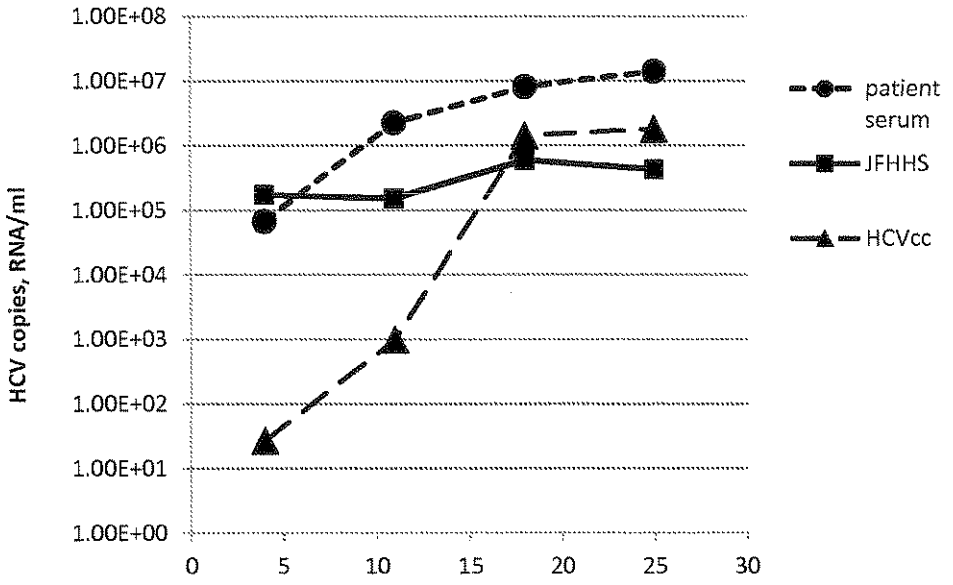
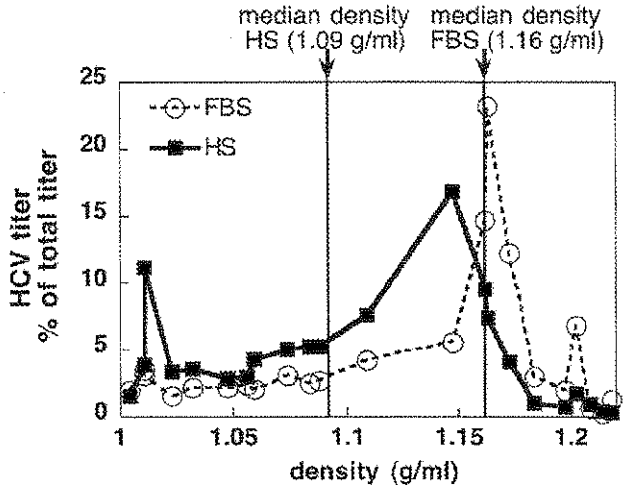
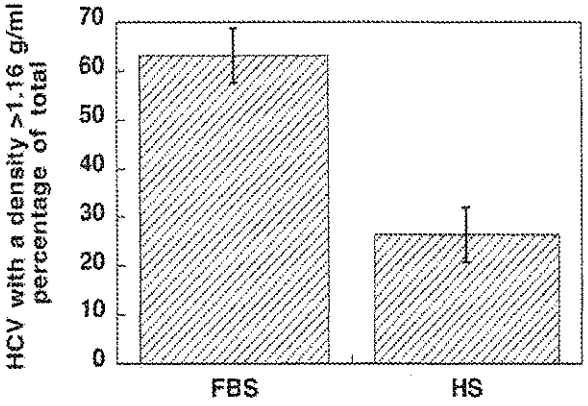

1.00E+08
1.00E+07
1.00E+06
1.00E+05
1.00E+04
1.00E+03
1.00E+02
1.00E+01
1.00E+00
HCV copies, RNA/ml
0
5
10
15
20
25
30
patient serum
JFHHS
HCVcc

Figure 8

A


median density HS (1.09 g/ml)
median density FBS (1.16 g/ml)
FBS
HS
HCV titer % of total titer
density (g/ml)
25
20
15
10
5
0
1
1.05
1.1
1.15
1.2

B


HCV with a density >1.16 g/ml percentage of total
70
60
50
40
30
20
10
0
FBS
HS

C

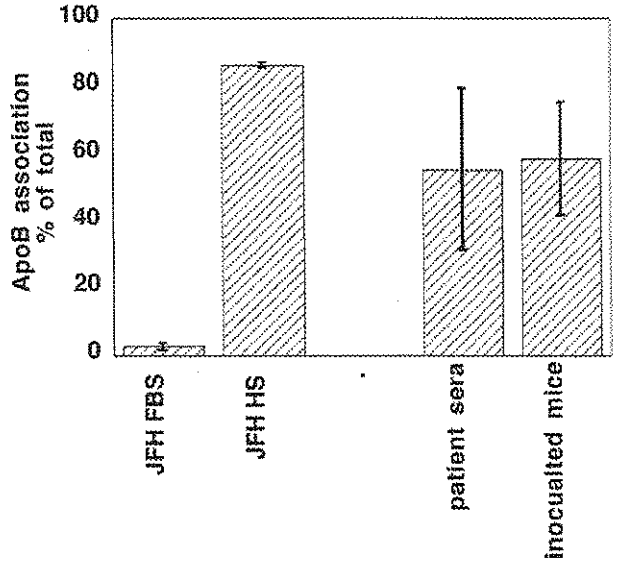

ApoB association % of total
100
80
60
40
20
0
JFH FBS
JFH HS
patient sera
inoculated mice

Figure 9

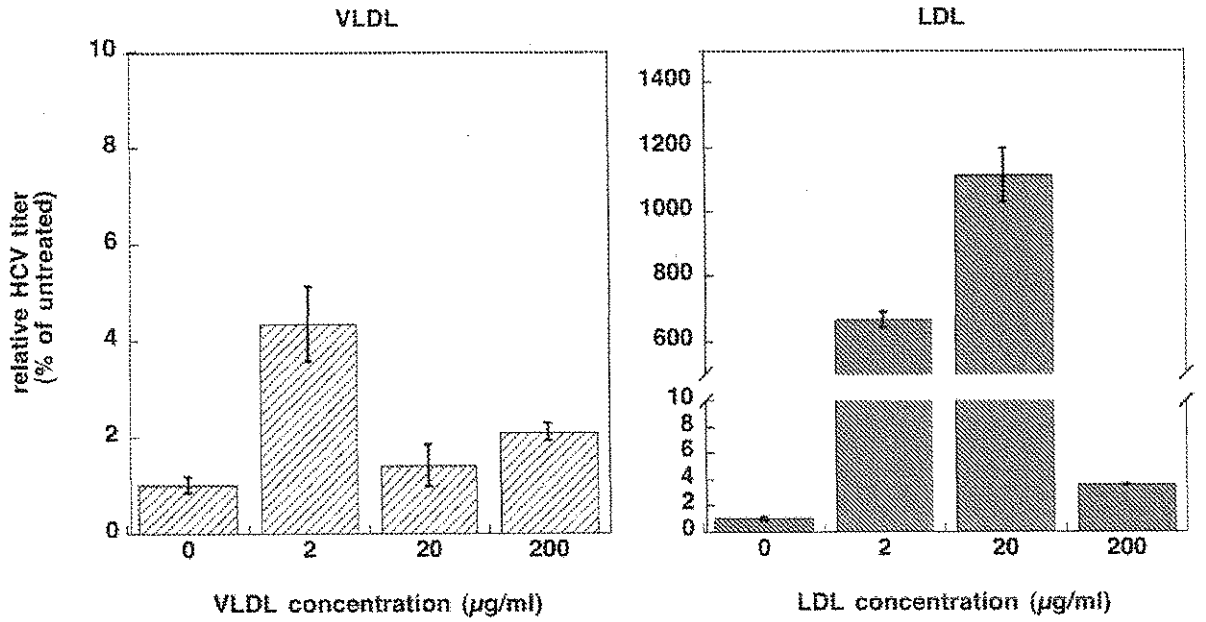

VLDL
LDL
relative HCV titer
(% of untreated)
10
8
6
4
2
0
1400
1200
1000
800
600
0
2
20
200
VLDL concentration (μg/ml)
LDL concentration (μg/ml)

Figure 10

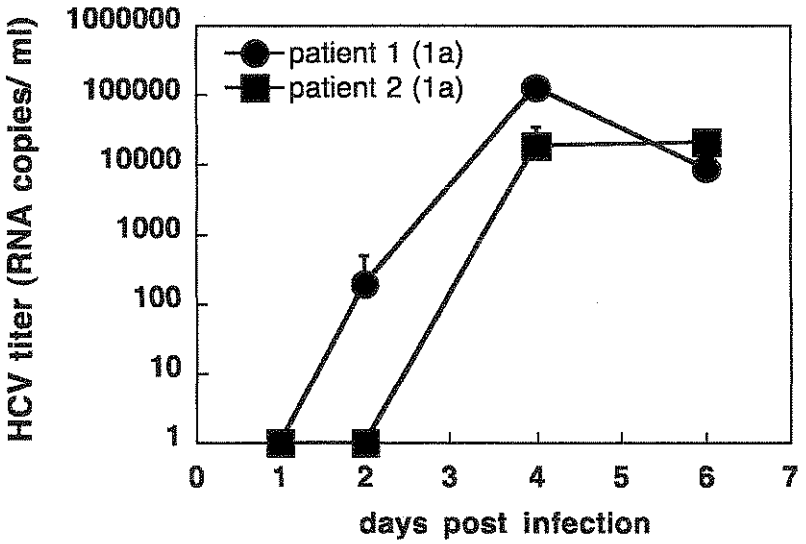

HCV titer (RNA copies/ ml)
1000000
100000
10000
1000
100
10
1
patient 1 (1a)
patient 2 (1a)
0
1
2
3
4
5
6
7
days post infection

Figure 11

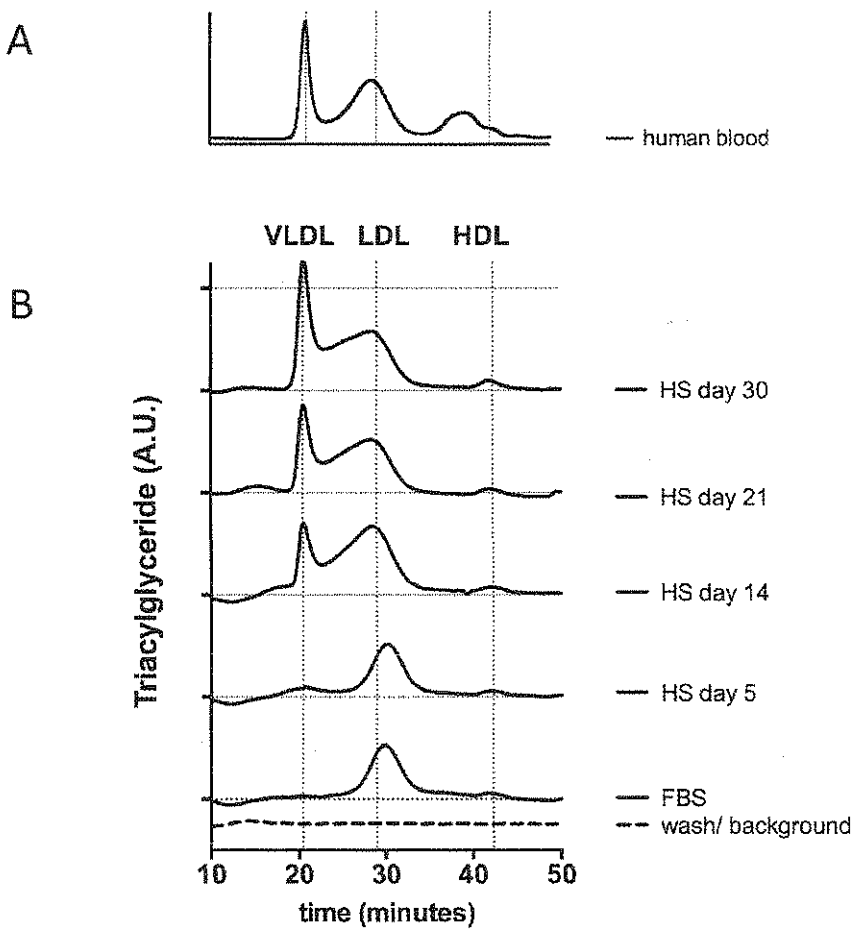

A
human blood
B
VLDL
LDL
HDL
Triacylglyceride (A.U.)
HS day 30
HS day 21
HS day 14
HS day 5
FBS
wash/ background
10
20
30
40
50
time (minutes)

Figure 12

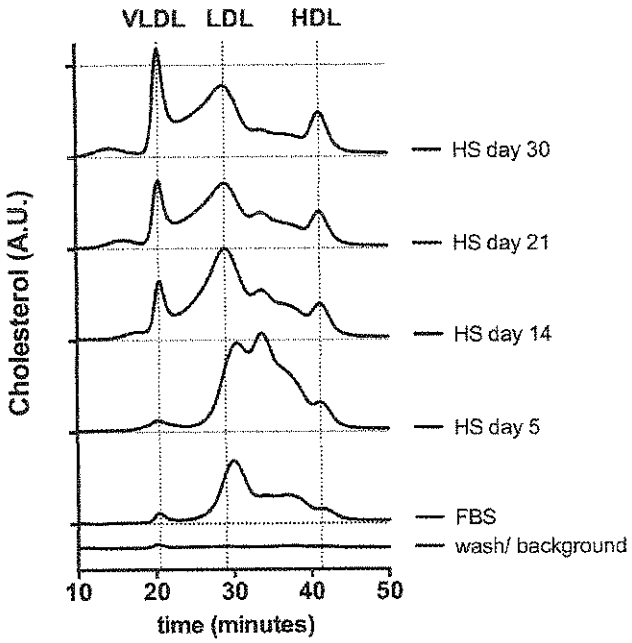

VLDL
LDL
HDL
Cholesterol (A.U.)
HS day 30
HS day 21
HS day 14
HS day 5
FBS
wash/ background
10
20
30
40
50
time (minutes)

Figure 13

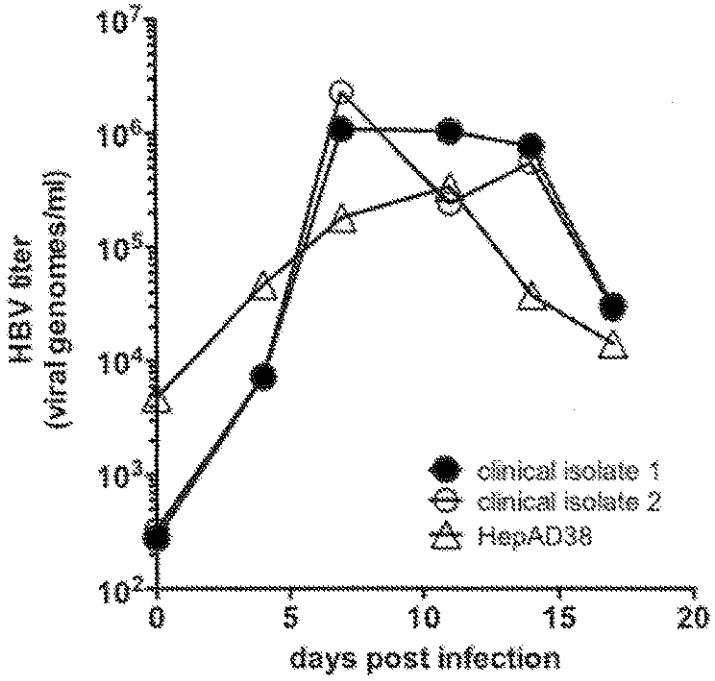

HBV titer
(viral genomes/ml)
10^7
10^6
10^5
10^4
10^3
10^2
0
5
10
15
20
days post infection
clinical isolate 1
clinical isolate 2
HepAD38

Figure 14

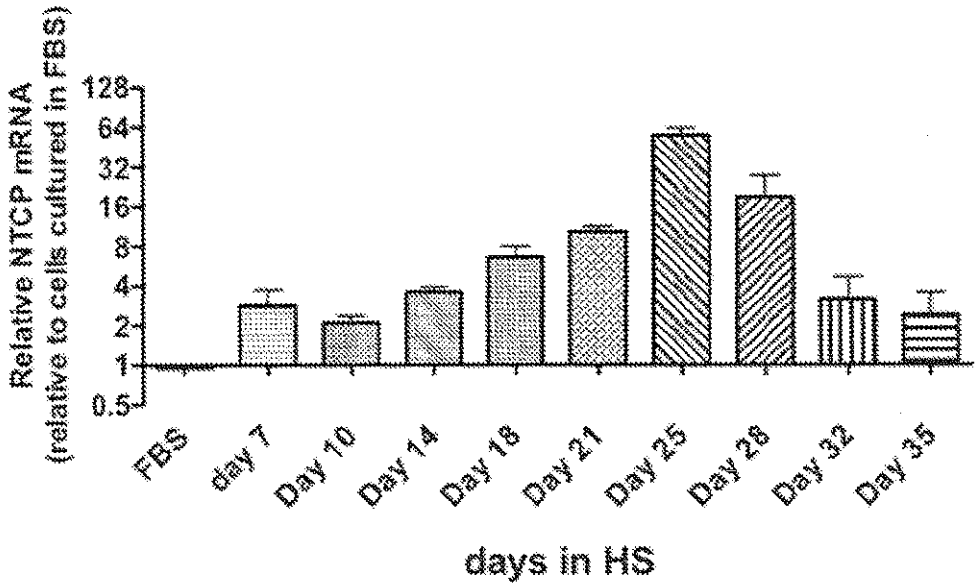

Relative NTCP mRNA
(relative to cells cultured in FBS)
128
64
32
16
8
4
2
1
0.5
FBS
day 7
Day 10
Day 14
Day 18
Day 21
Day 25
Day 28
Day 32
Day 35
days in HS

Figure 15

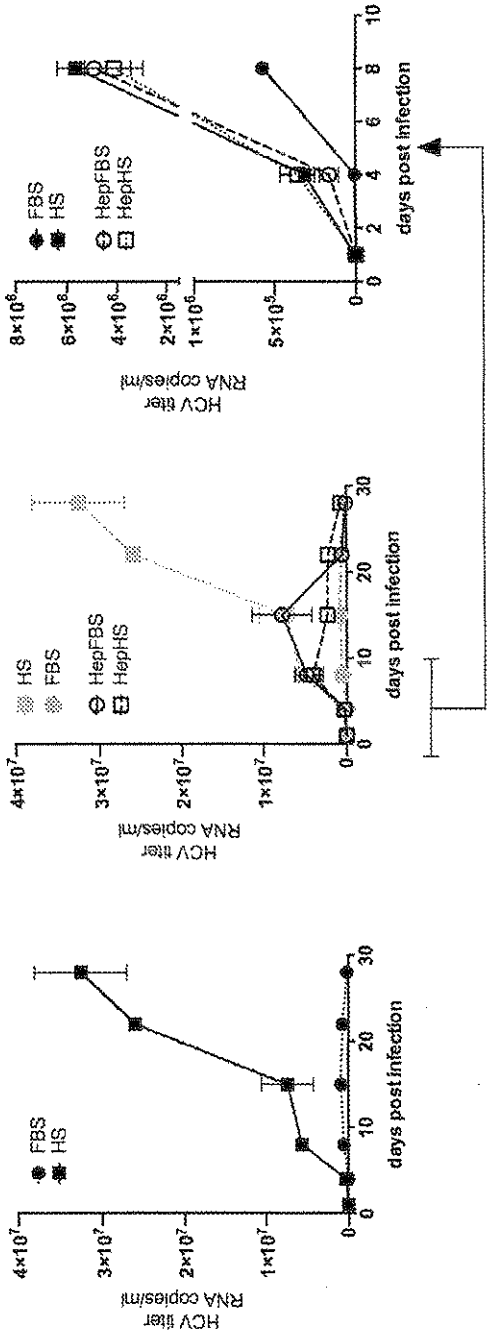

A
B
C
FBS
HS
HepFBS
HepHS
HCV titer
RNA copies/ml
days post infection
4×10^7
3×10^7
2×10^7
1×10^7
0
10
20
30
8×10^6
6×10^6
4×10^6
2×10^6
1×10^6
5×10^5
2
4
6
8

Figure 16

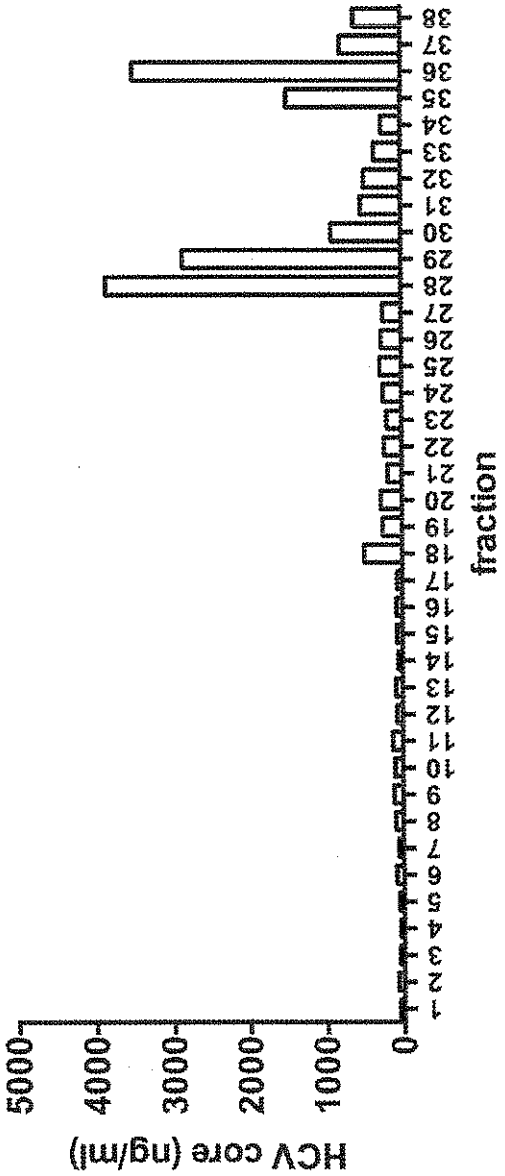

HCV core (ng/ml)
5000
4000
3000
2000
1000
0
fraction
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38

Figure 17

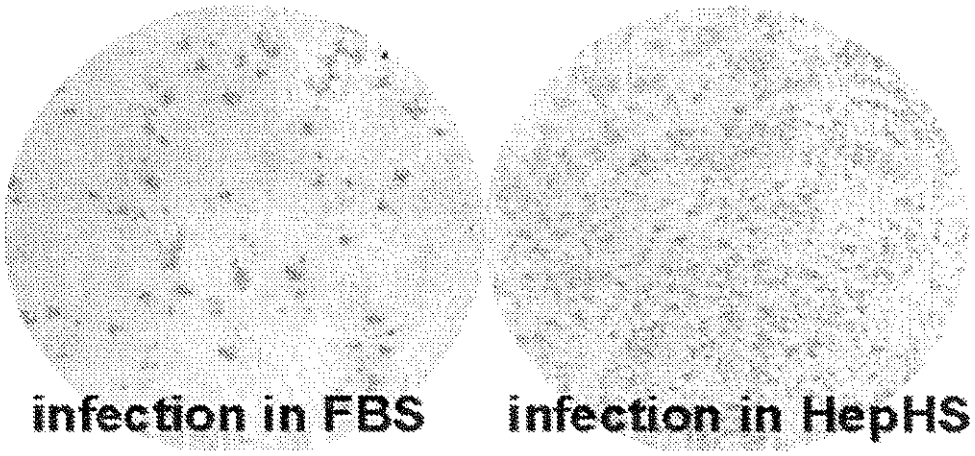


Figure 18

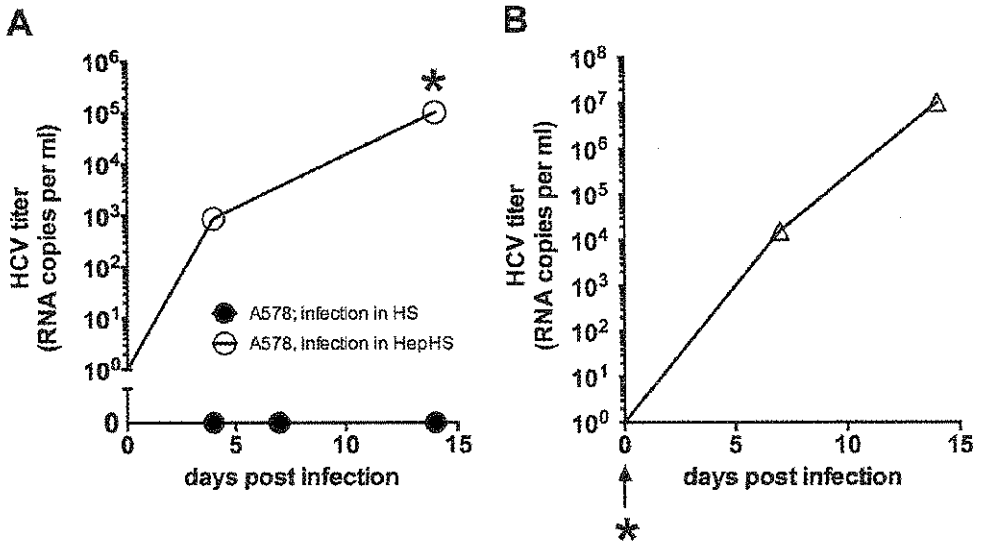

A
HCV titer
(RNA copies per ml)
10^6
10^5
10^4
10^3
10^2
10^1
10^0
0
*
A578; infection in HS
A578, infection in HepHS
0
5
10
15
days post infection
B
HCV titer
(RNA copies per ml)
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
0
5
10
15
days post infection
*

Figure 19

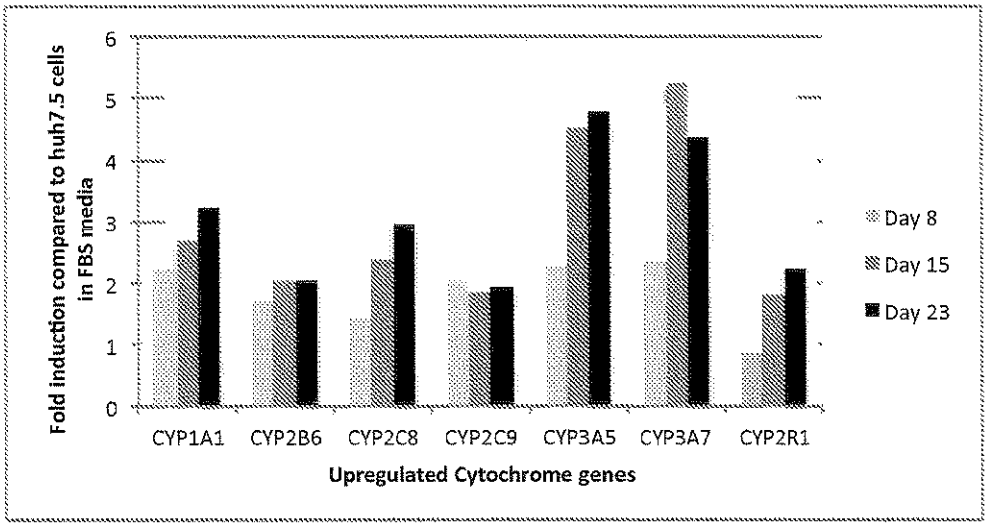


Figure 20

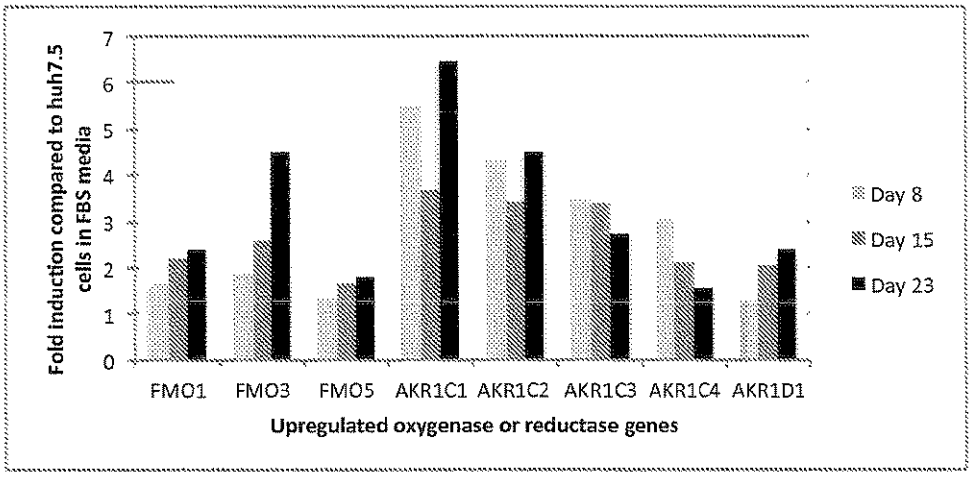


Figure 21

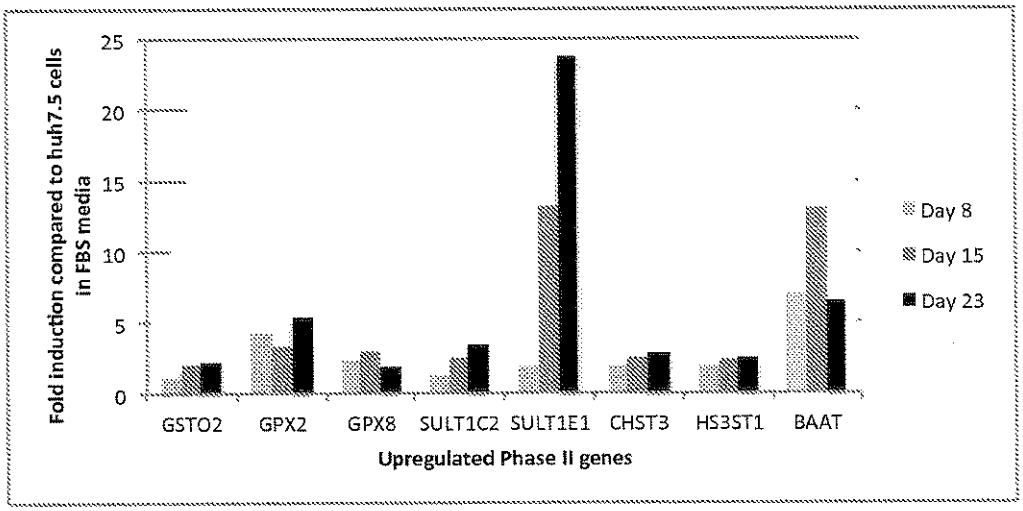


Figure 22

