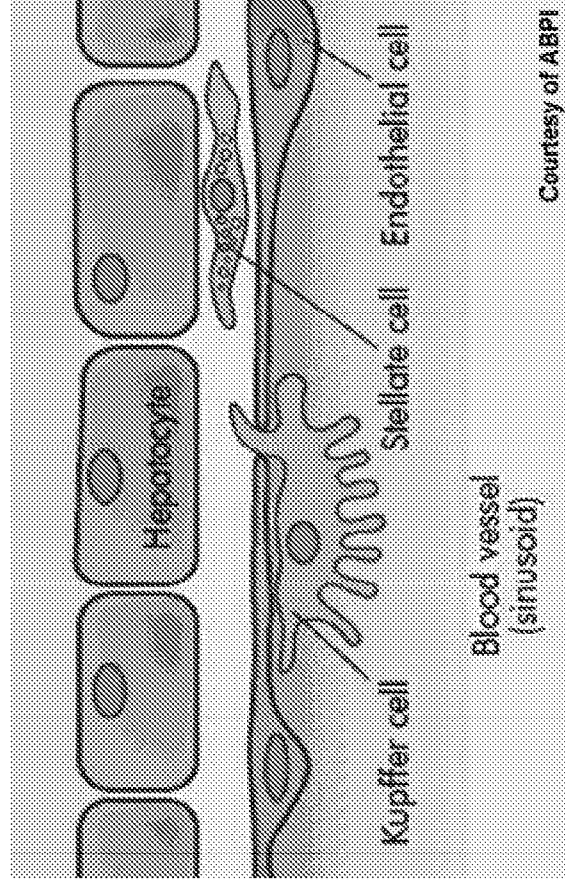
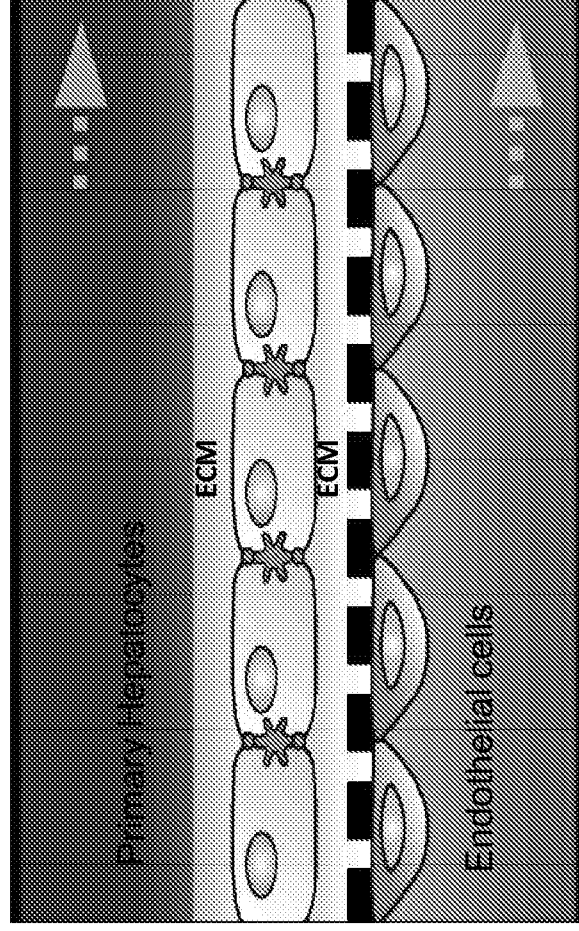


Figs. 1A-1B

A



B



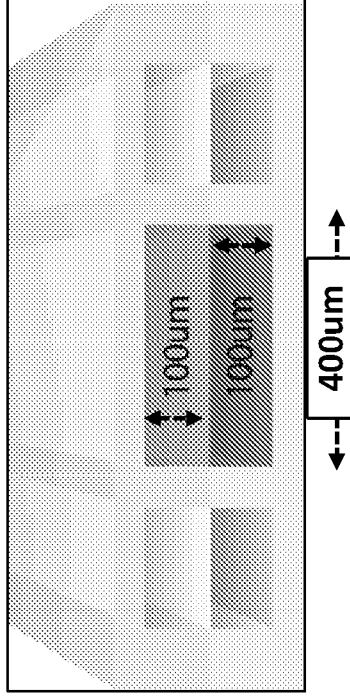
Schematic of Human Liver Structure

Liver-on-a-Chip Design

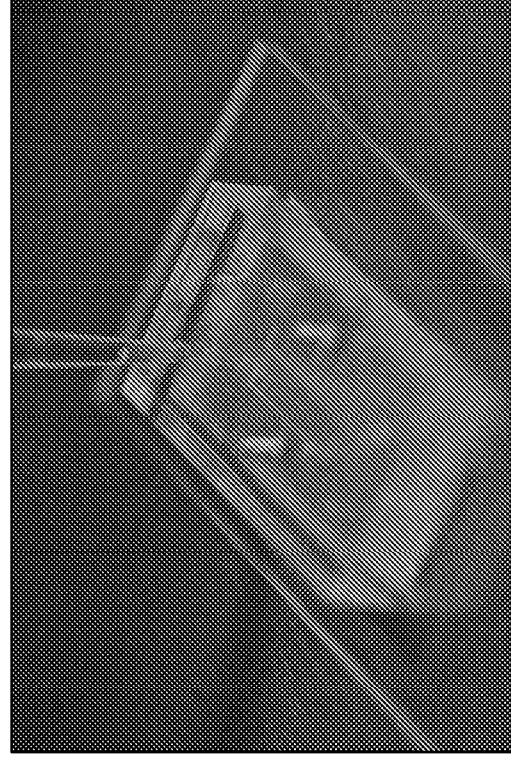
Figs. 2A-2D

A

Embodiment 1



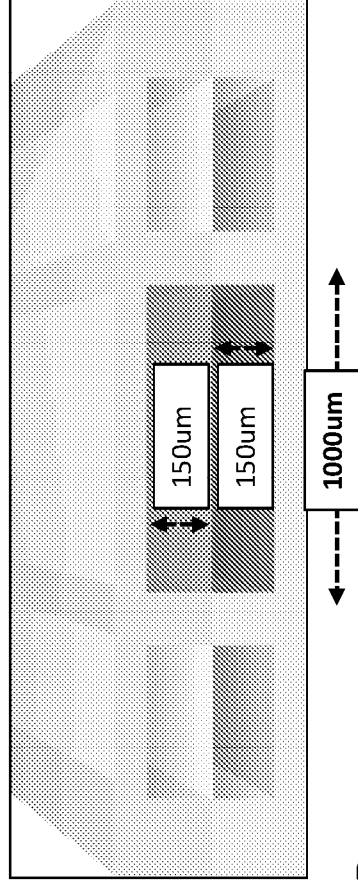
C



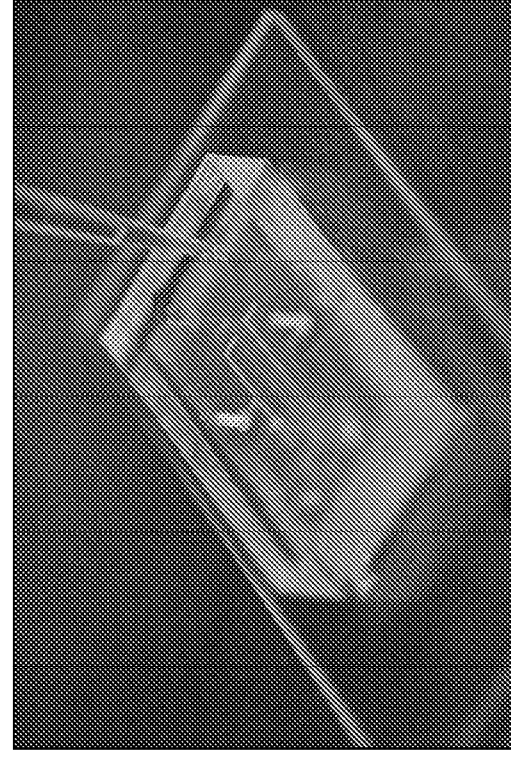
Seeding of Hepatocytes

B

Embodiment 2



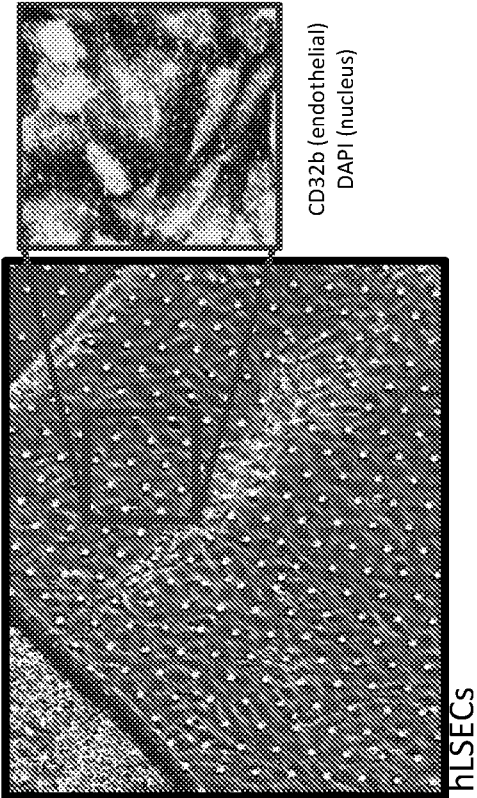
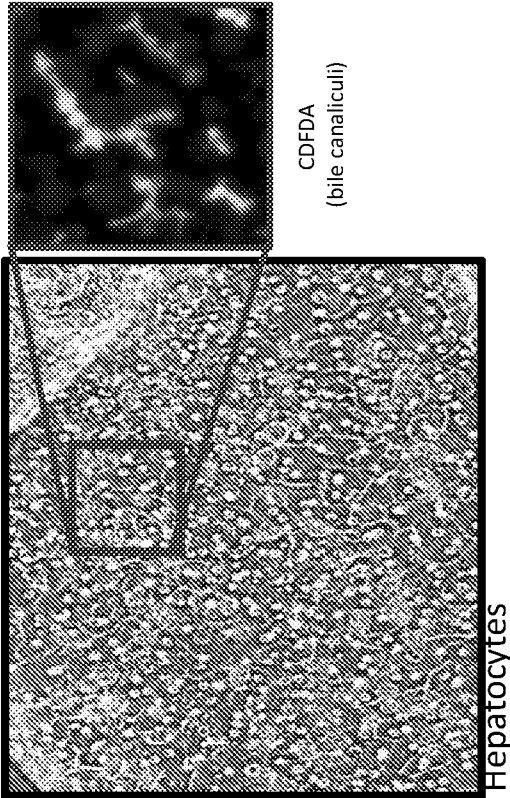
D



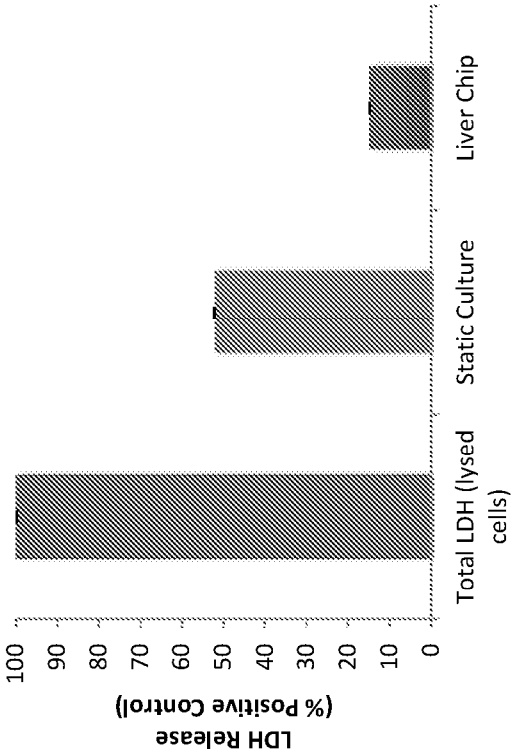
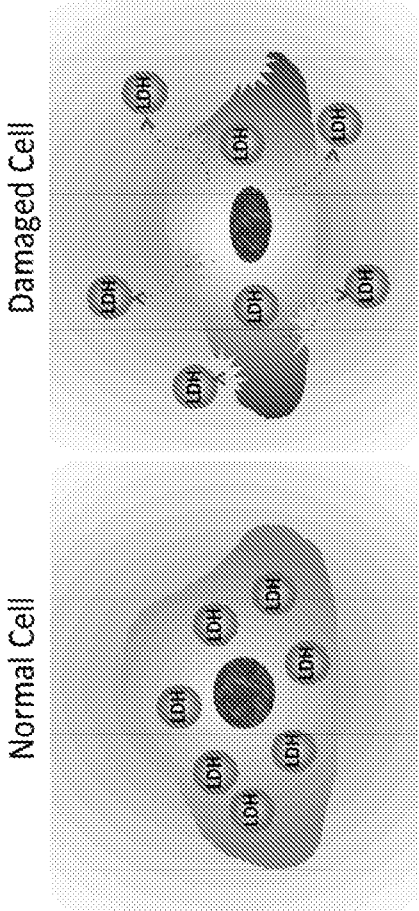
Seeding of hLSECS

Figs. 3A-3B

A Morphology



B Cell Viability (LDH Release)



Figs. 4A-4B

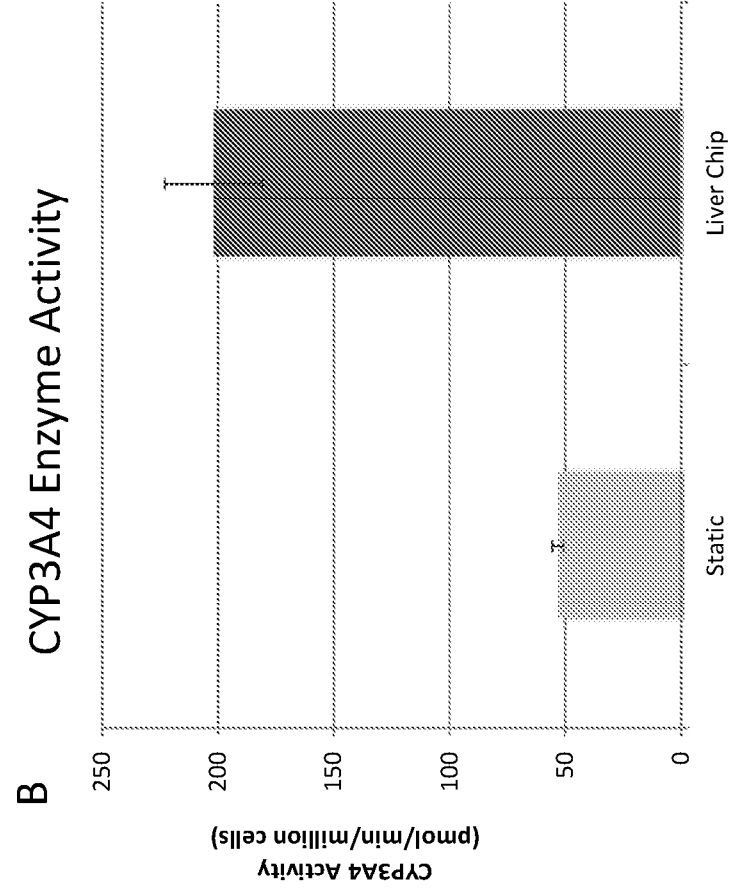
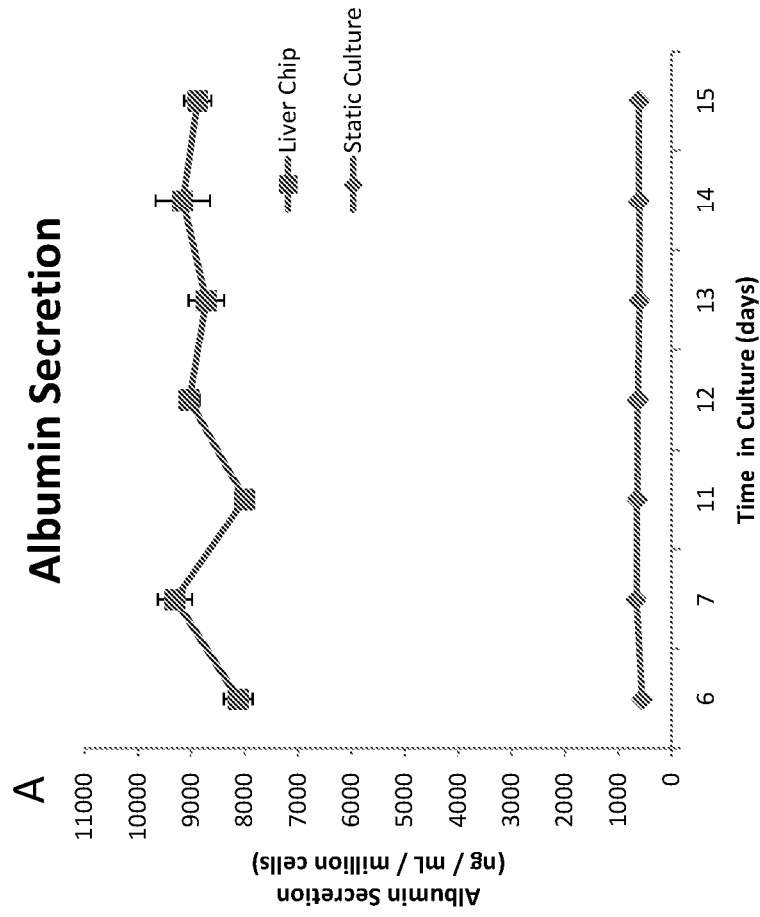
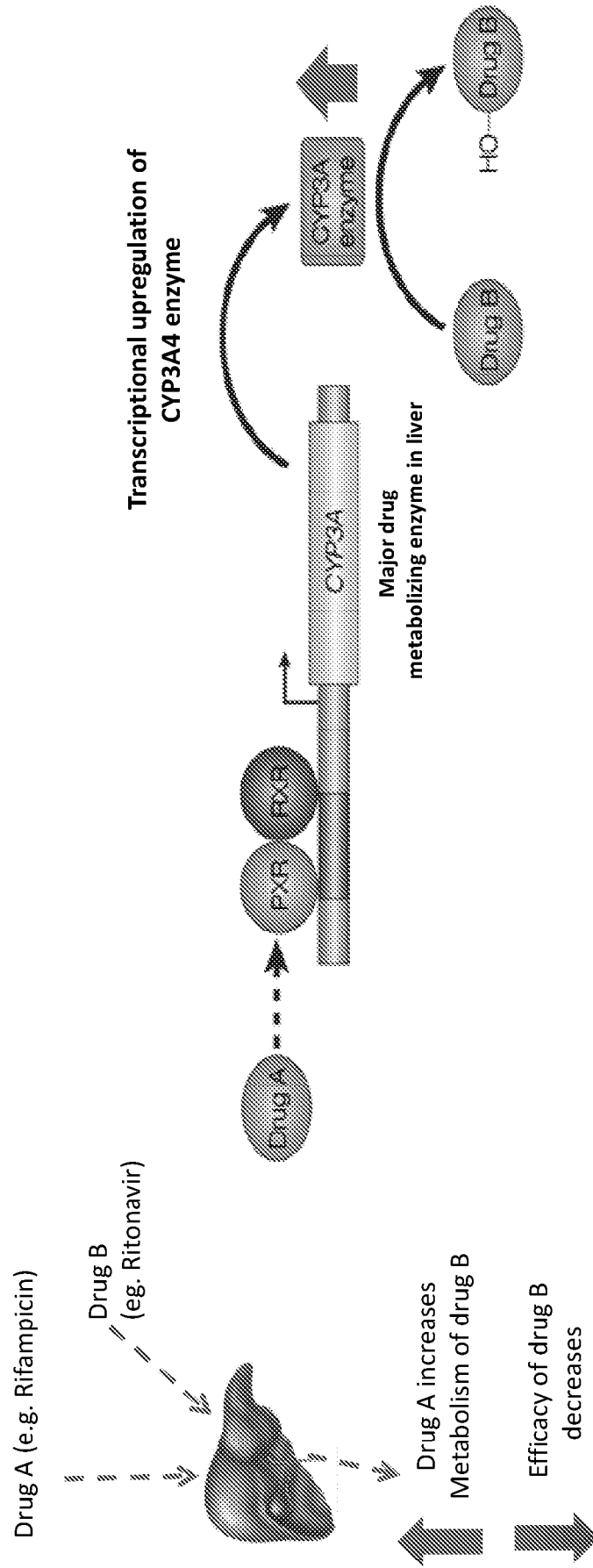
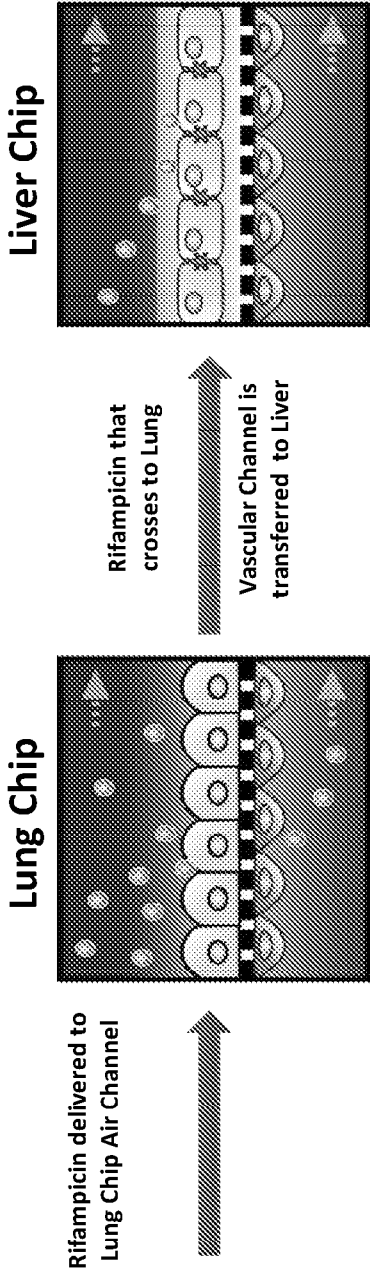


Fig. 5



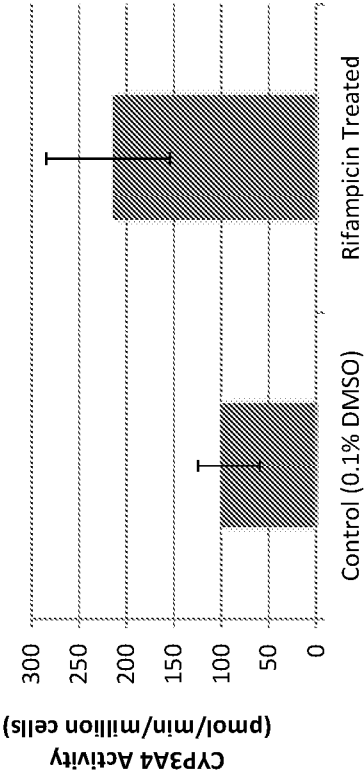
Figs. 6A-6B

A



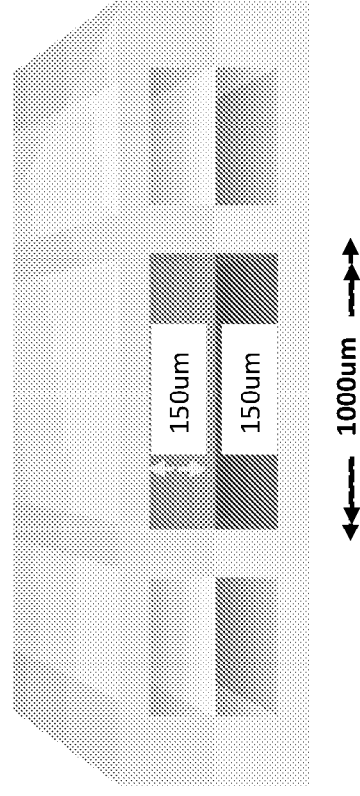
B

Drug treatment in the Lung Chip caused CYP3A4 Induction in Liver

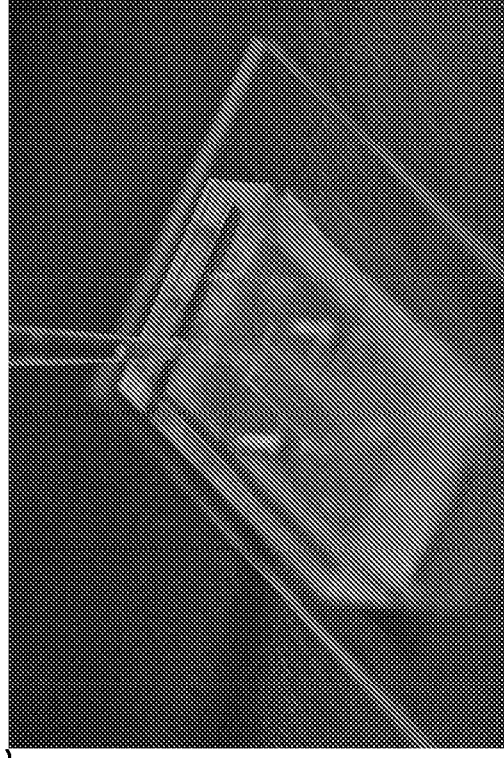


Figs. 7A-7D

A Liver-on-Chip v1



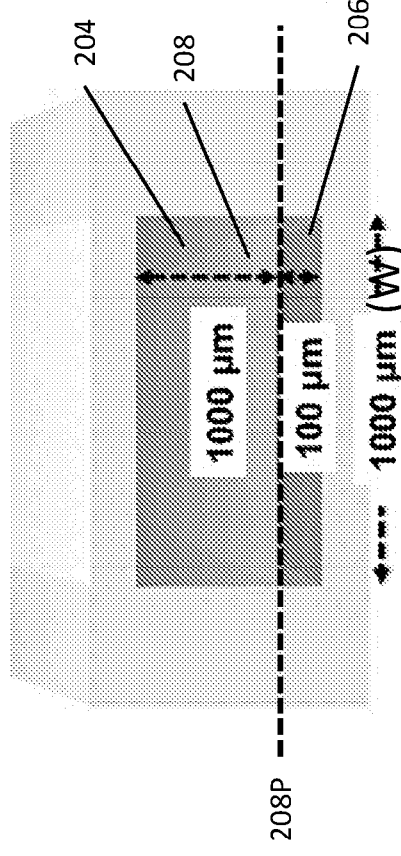
C



Seeding of Hepatocytes

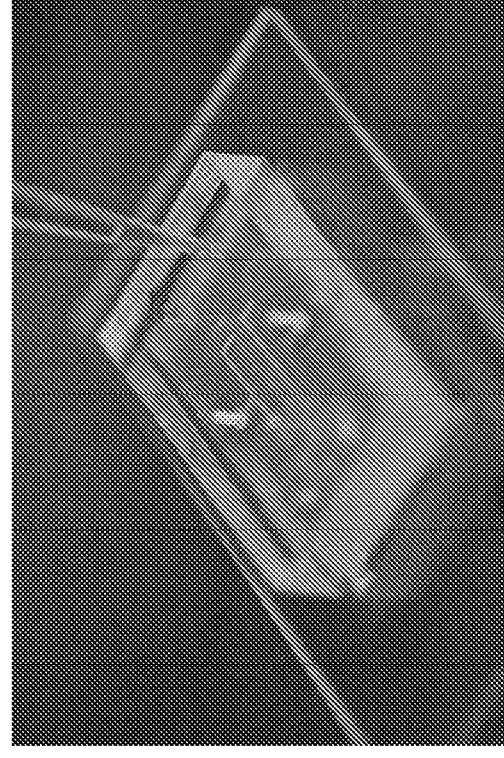
B Liver-on-Chip v2

200



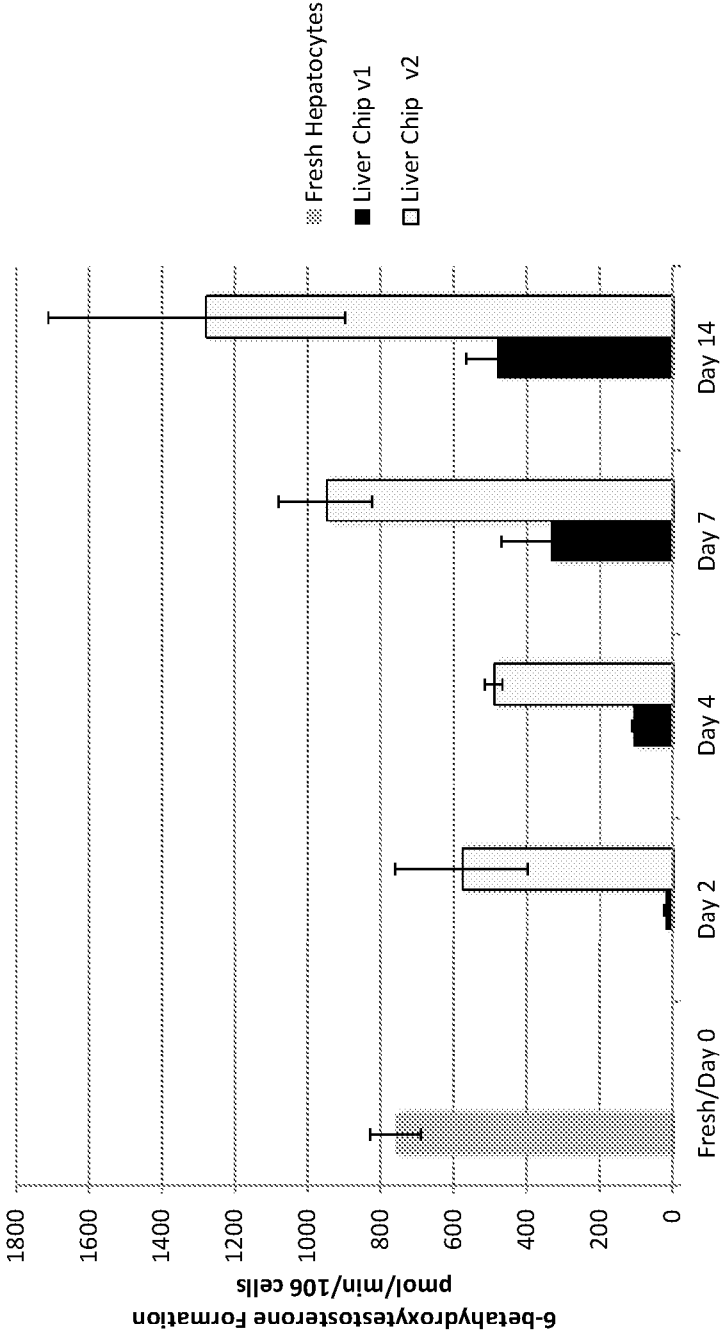
208P

D



Seeding of hLSECS

Fig. 8
CYP 3A4 Activity For Human Lot8150



Figs. 9A-9B

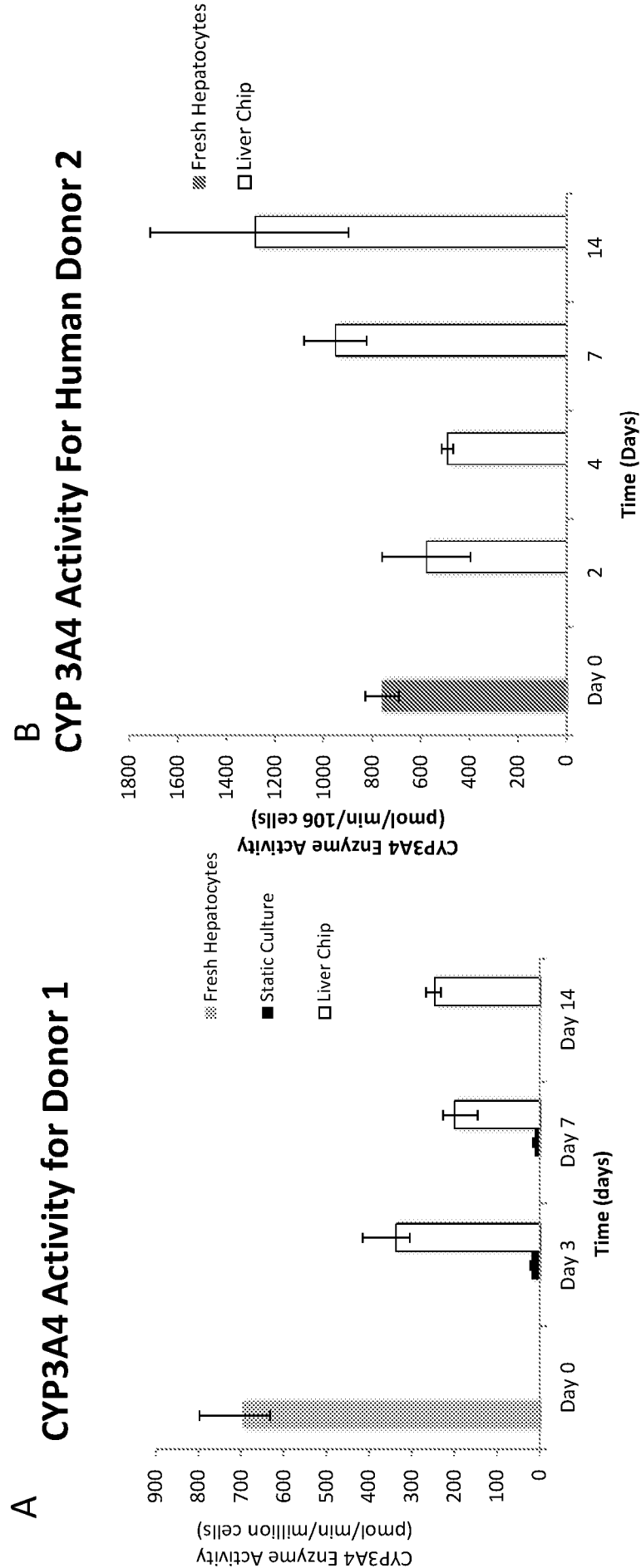


Fig. 10

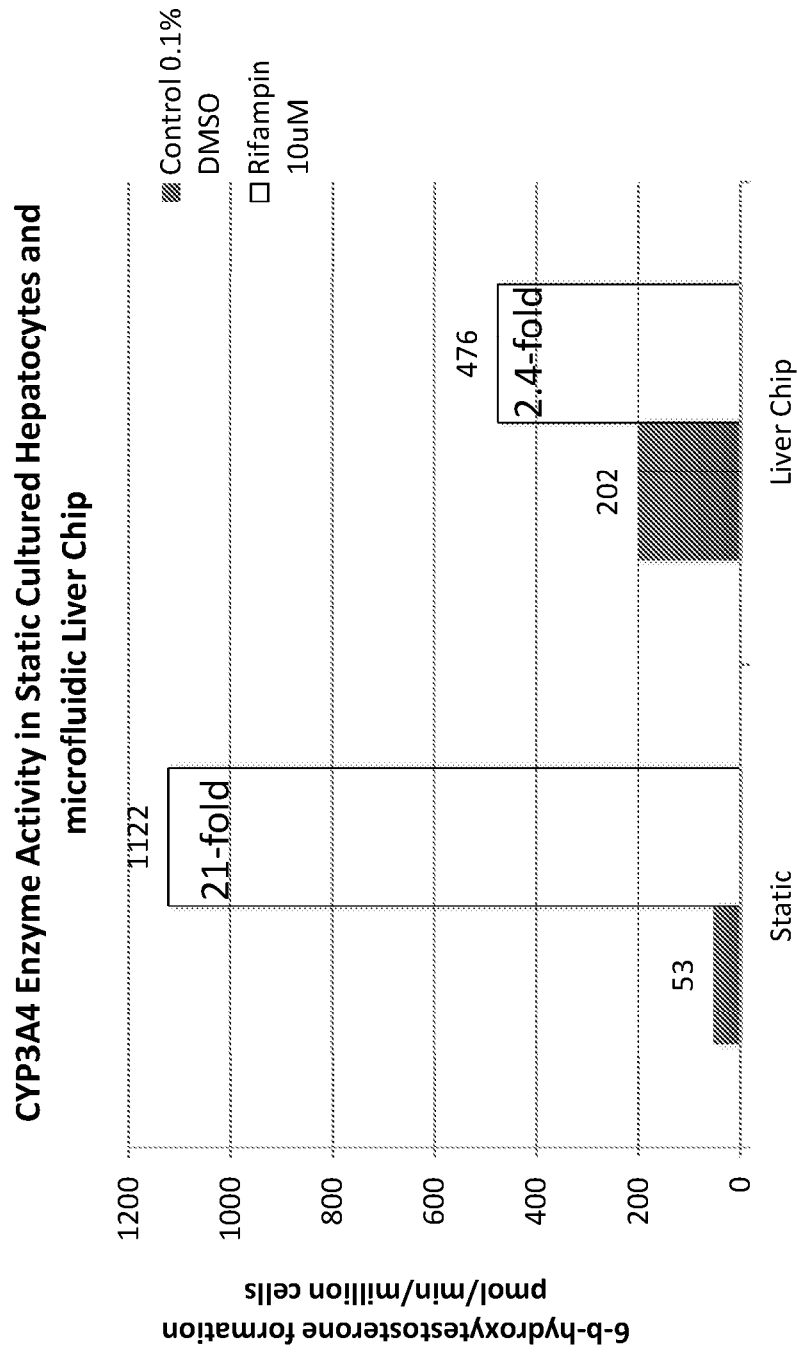
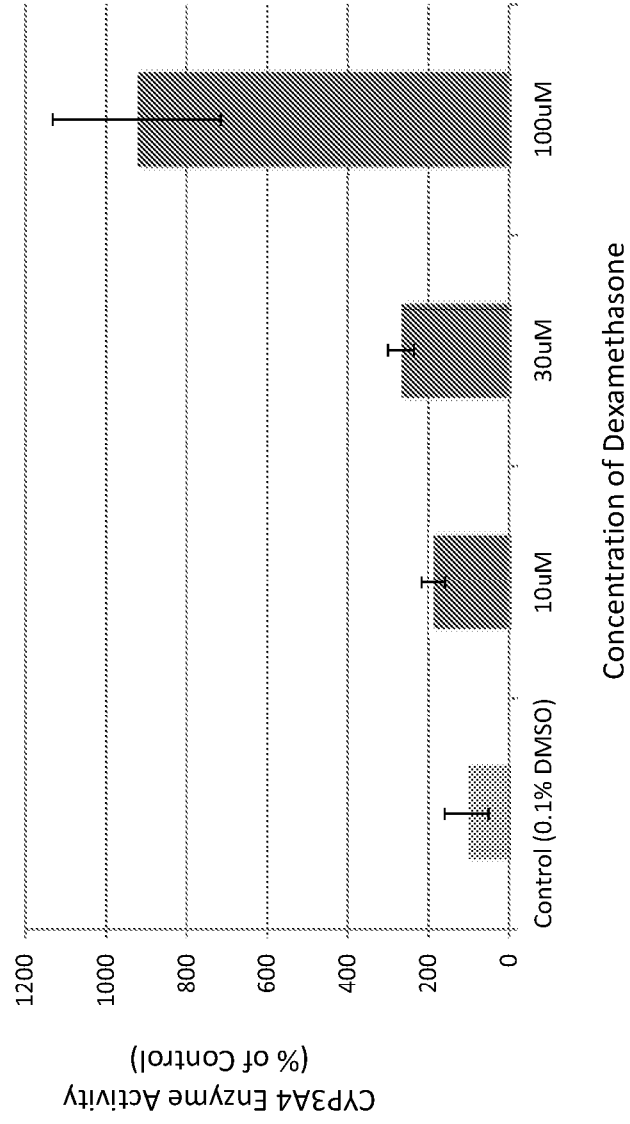
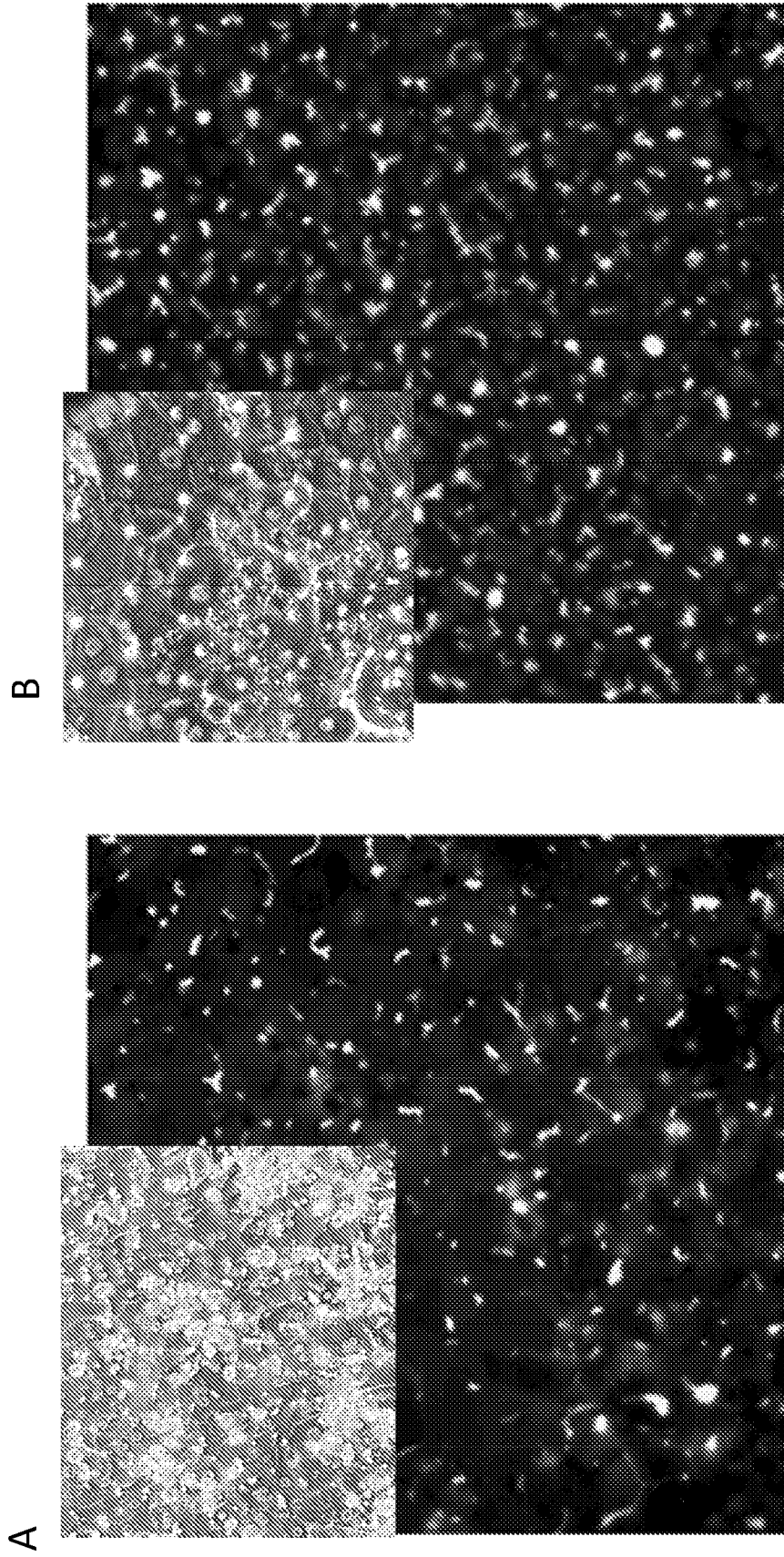


Fig. 11

CYP3A4 Induction by Dexamethasone in Liver-on-Chip



Figs. 12A-12B



Figs. 13A-13B

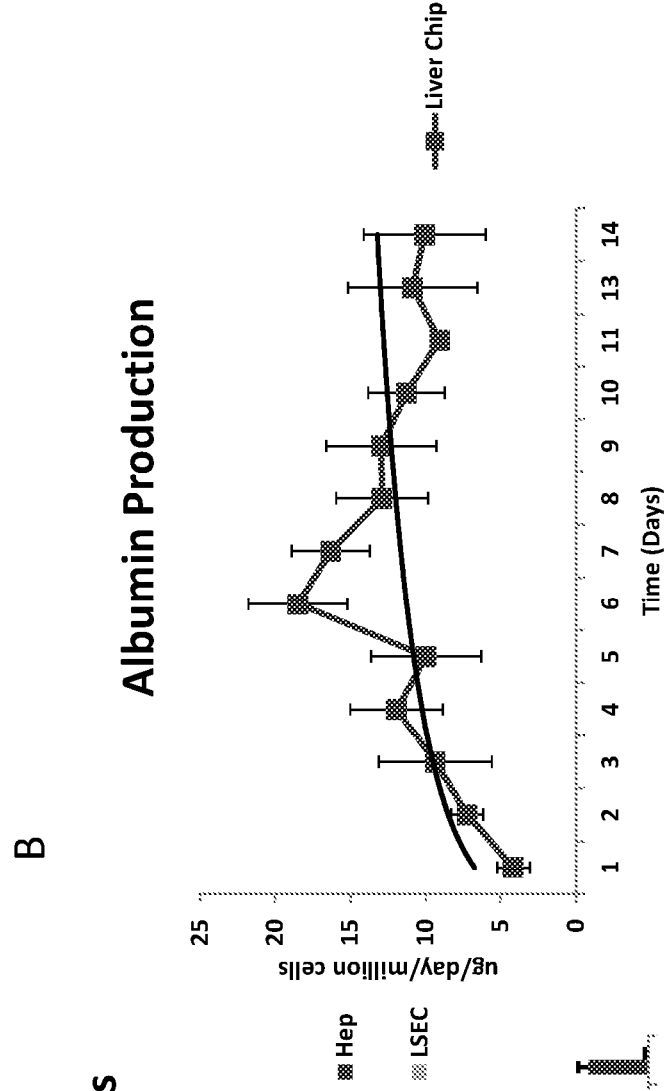
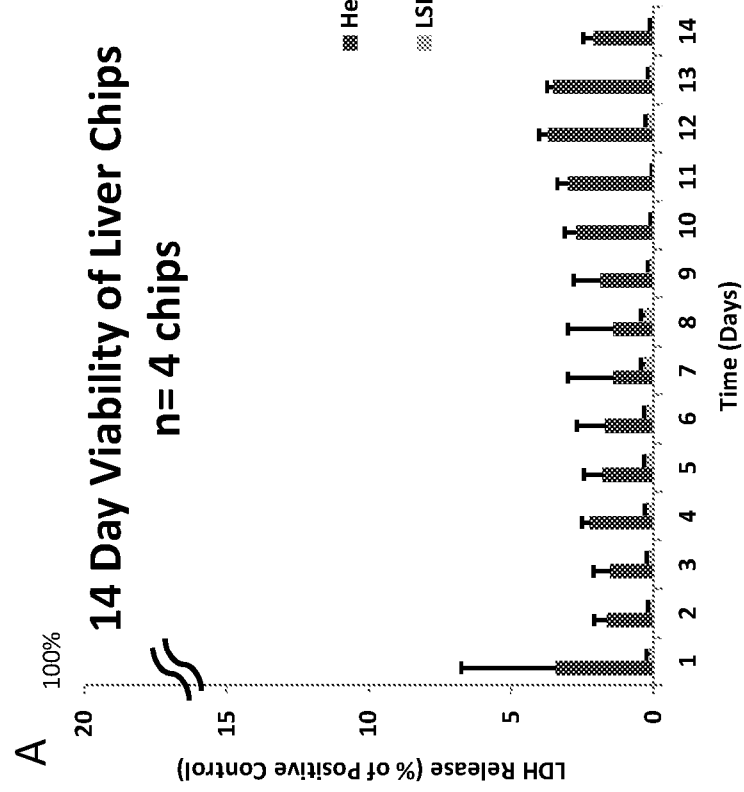
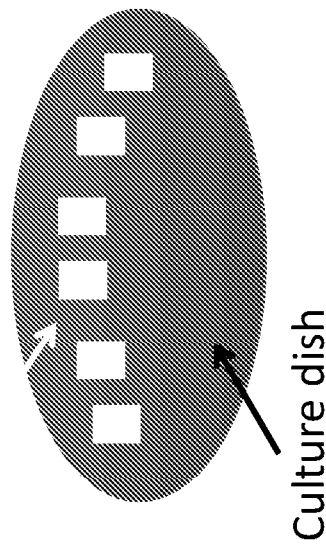


Fig. 14A

PDMS with different conditions



1 PDMS Surface treatment

- Plasma
- APTES

3 ECM Overlay

- Matrigel vs Mixture of Matrigel+ Fibronectin

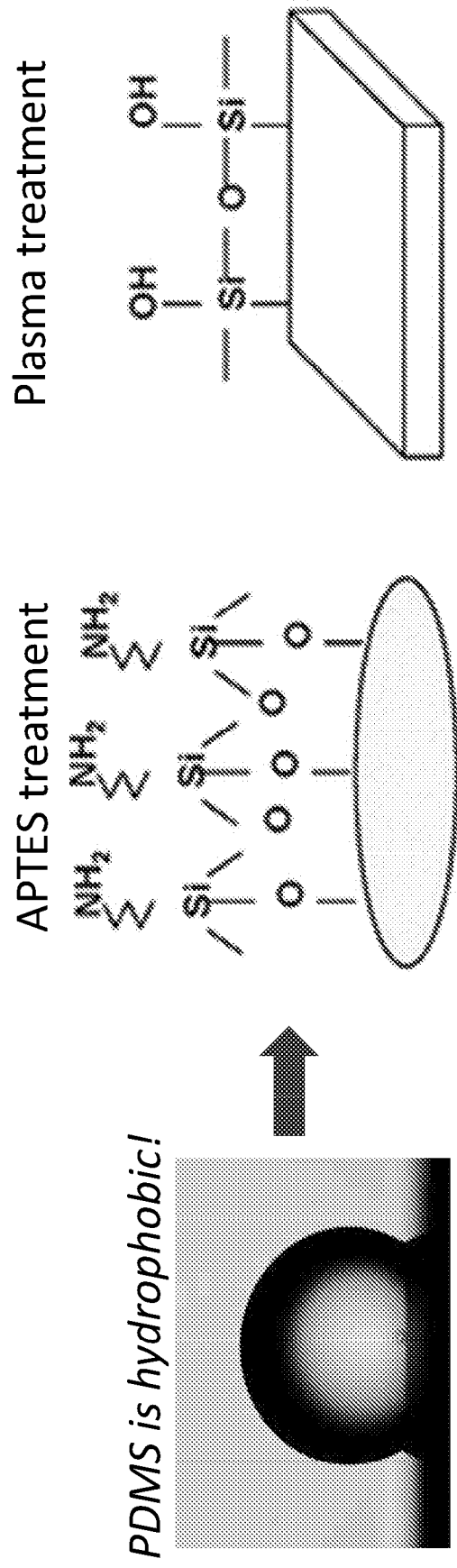
2 ECM Coating

ECM	Concentration (mg/ml)
Collagen I	1, 0.5, 0.5+Matrigel 0.1
Fibronectin	1, 0.5, 0.5 +Matrigel 0.1
Collagen IV	1
Mixture	Col I+Col IV+FN

4 Medium

Basal Medium	Supplement
WEM complete	10% FBS
(William's E medium + L- Glutamax, ITS +, Dexamethasone, Penn/Strep)	SBTI (Soybean Trypsin Inhibitor) 1mg/ml
	EGF (Epidermal growth factor) 200ng/ml

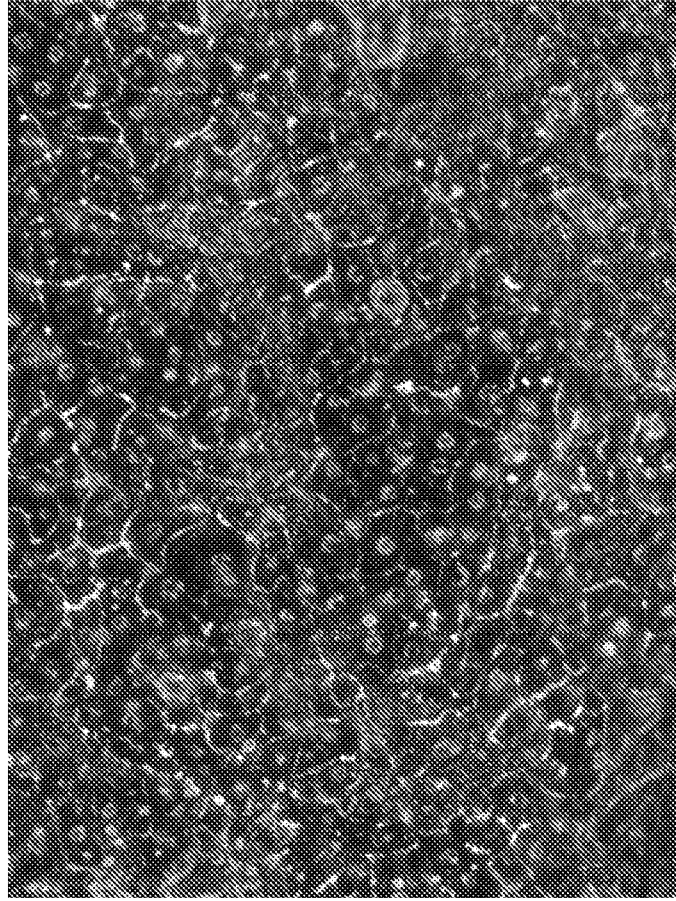
Fig. 14B
PDMS Surface Treatment



Figs. 15A-15B

A

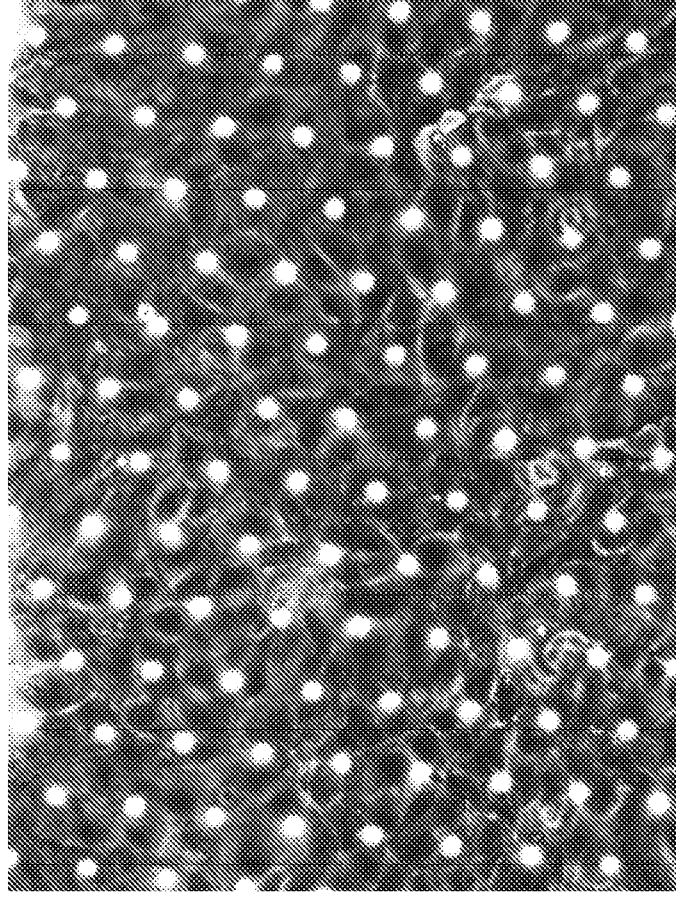
Hepatocytes



Day 14

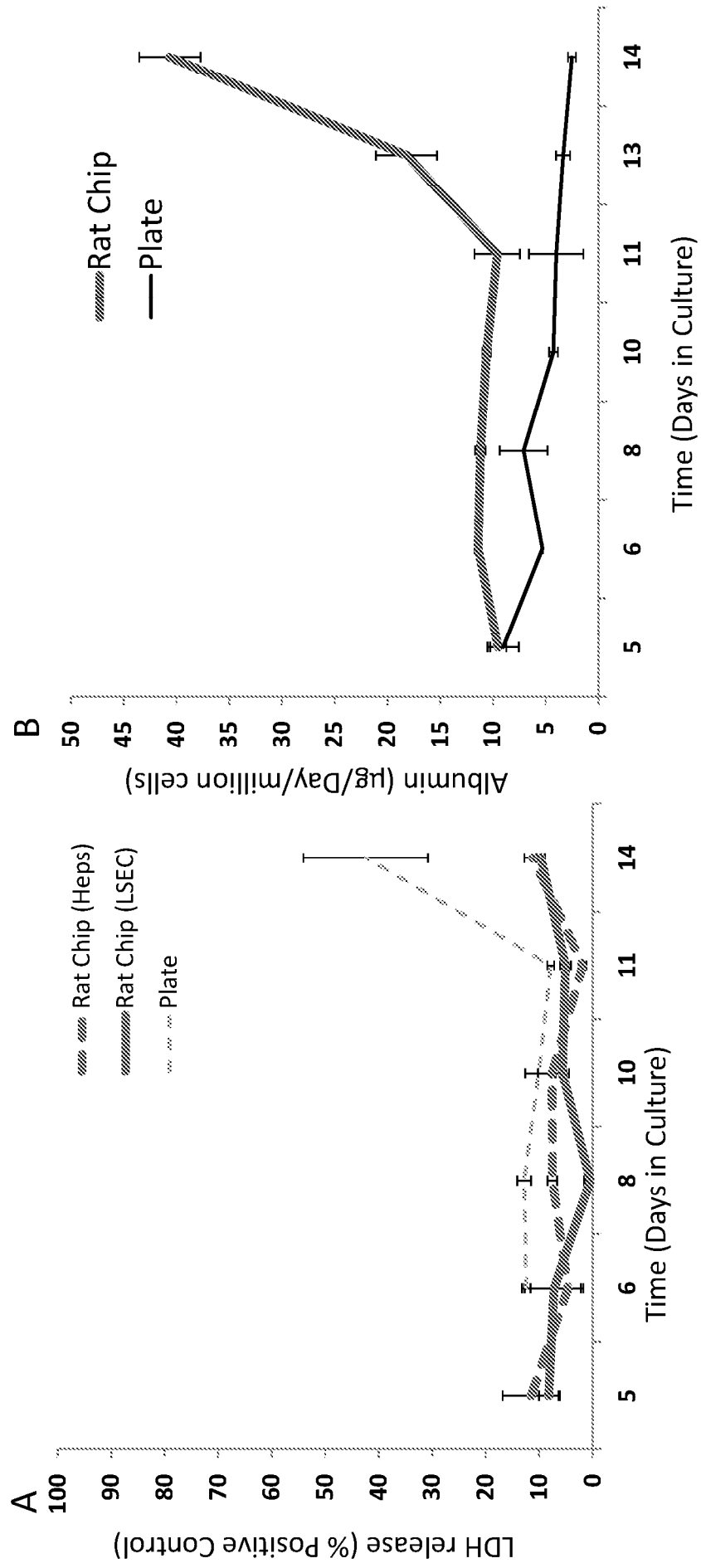
B

LSECs



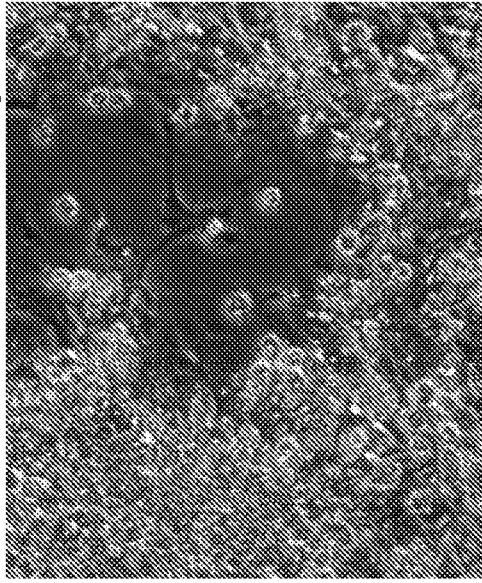
Day 14

Figs. 16A-16B



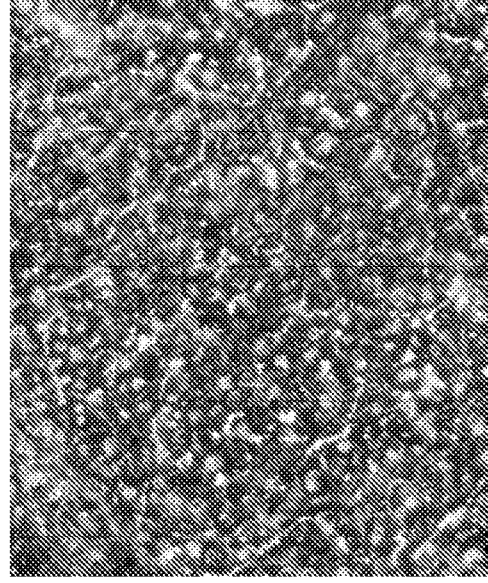
Figs. 17A-17C

A Static Culture –Plate Day 28

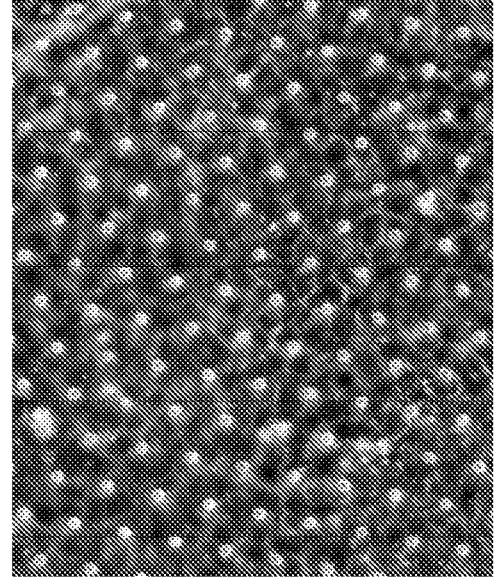


B

Rat Liver Chip –Day 28

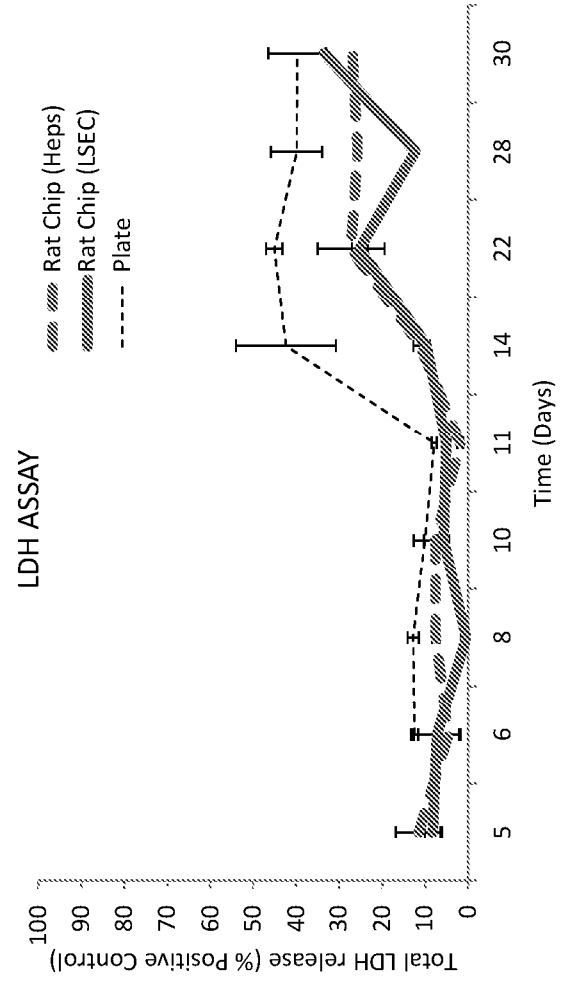


Hepatocytes



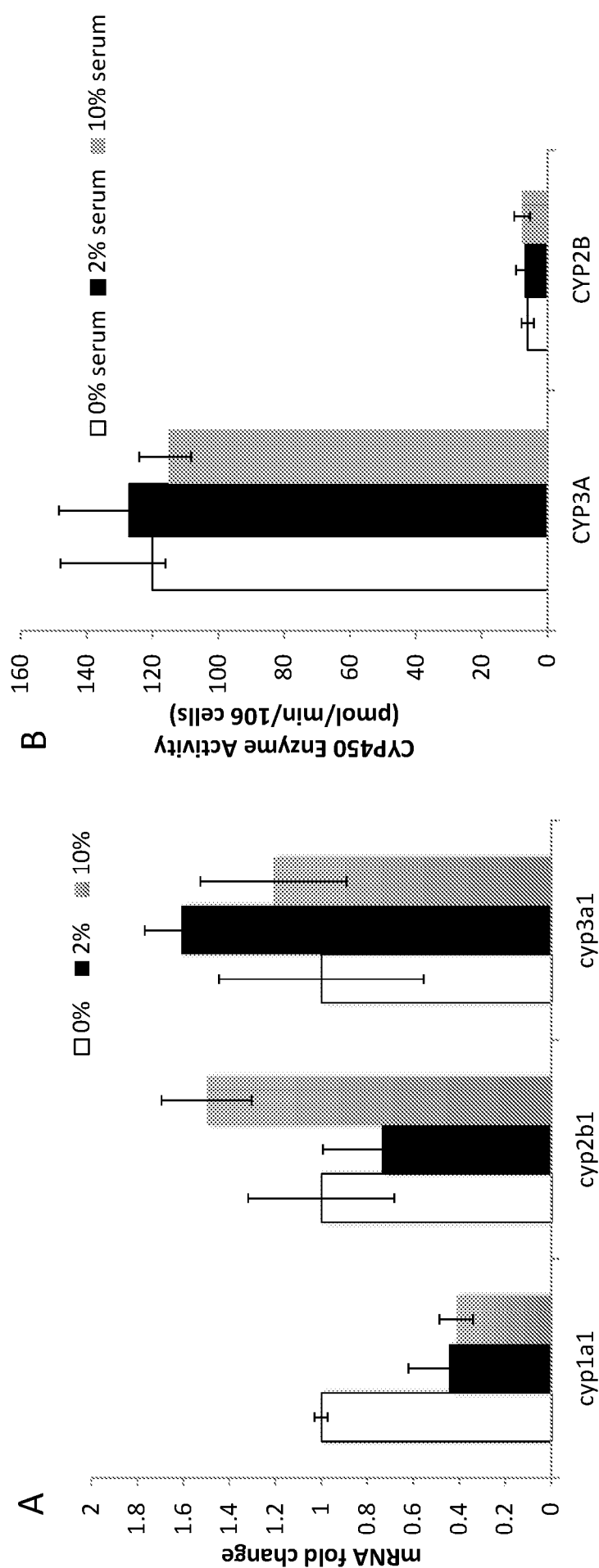
rLSECs

C



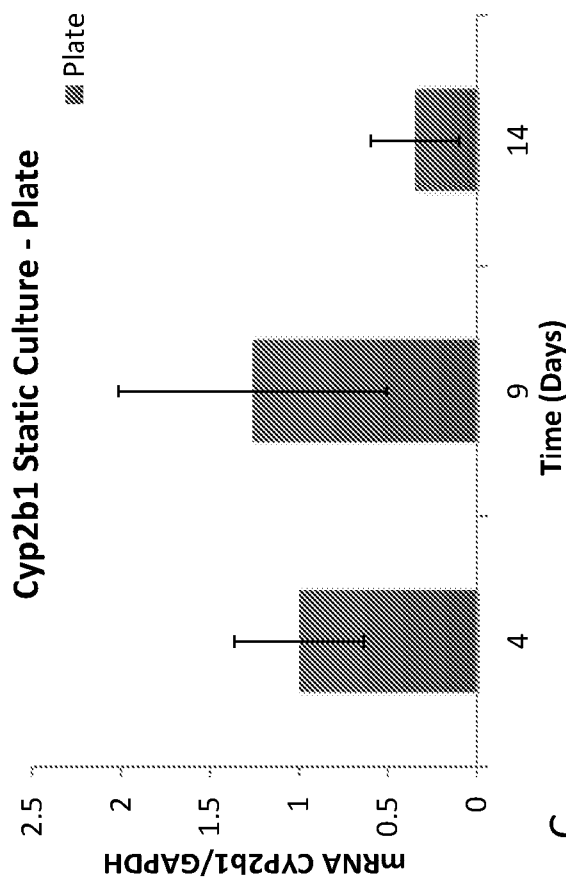
Figs. 18A-18B

Rat Hepatocytes in Conventional Sandwich Plate Culture (Day 7)

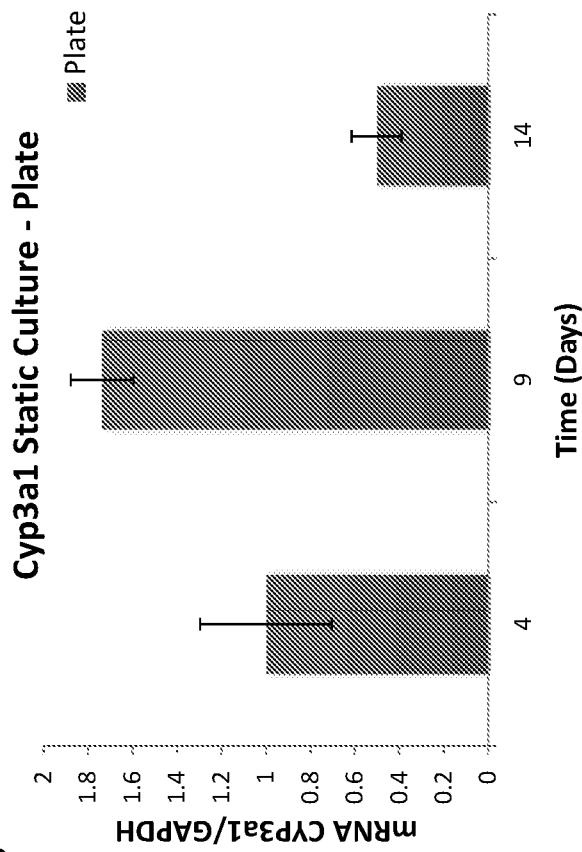


Figs. 19A-19C

A



B



C

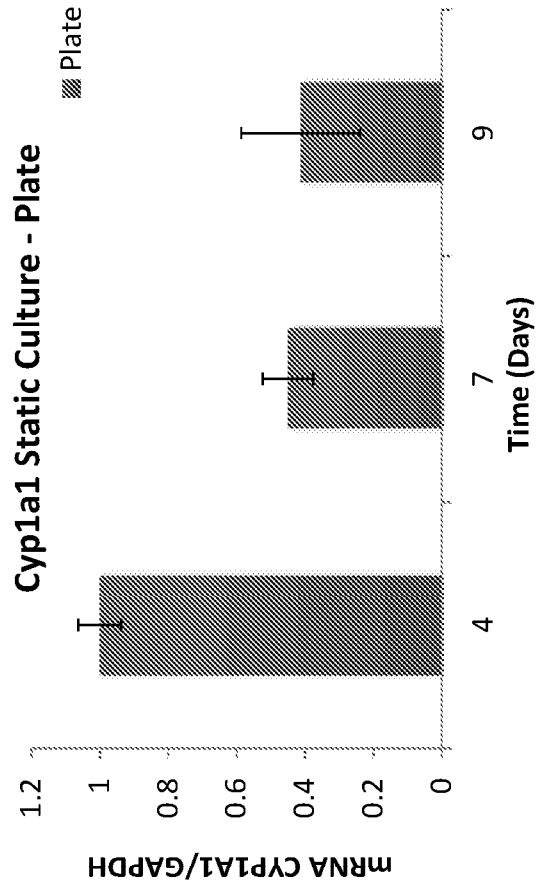


Fig. 20A

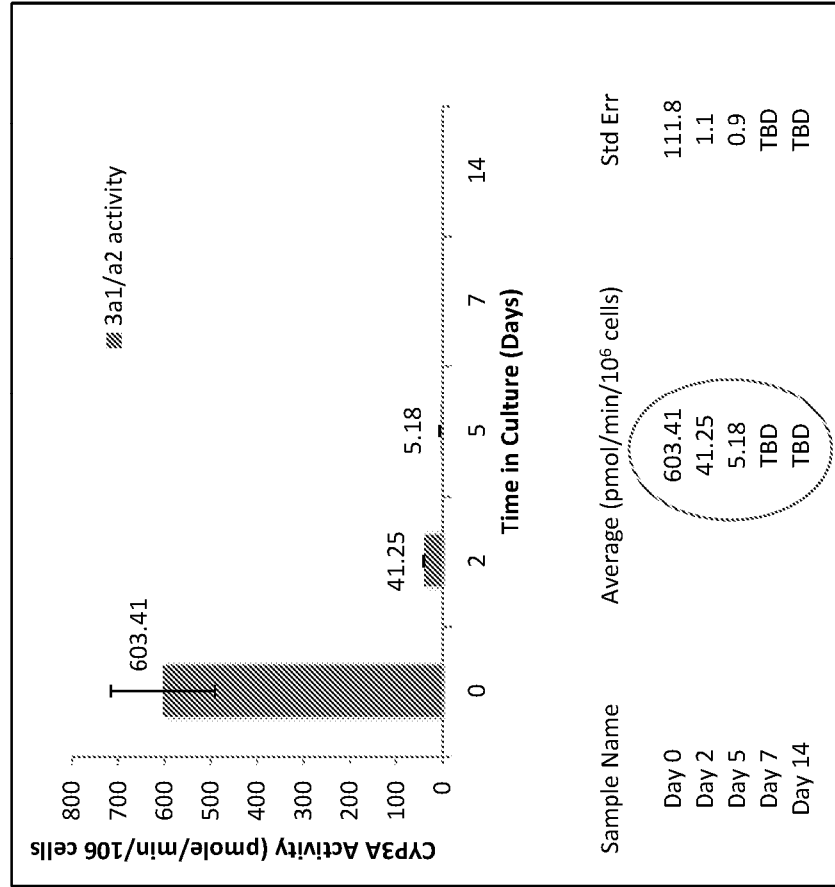
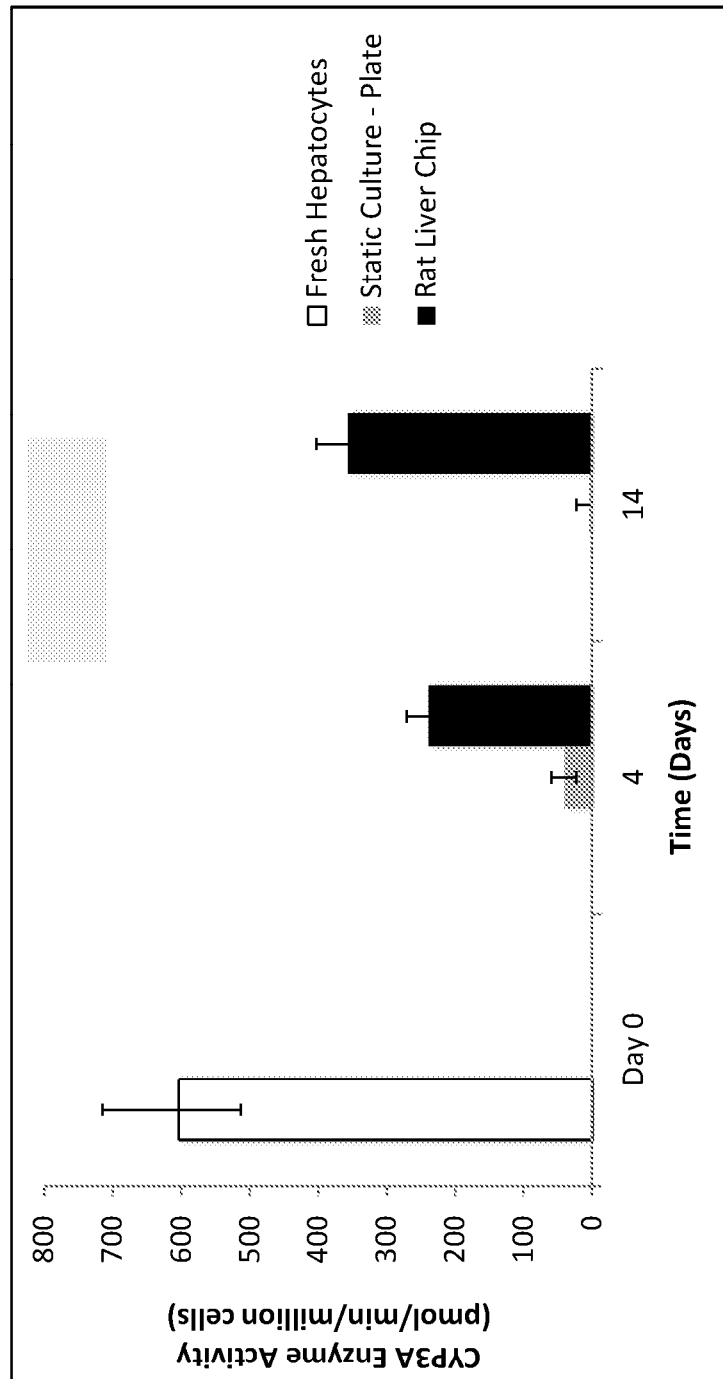


Fig. 20B



Figs. 21A-21C

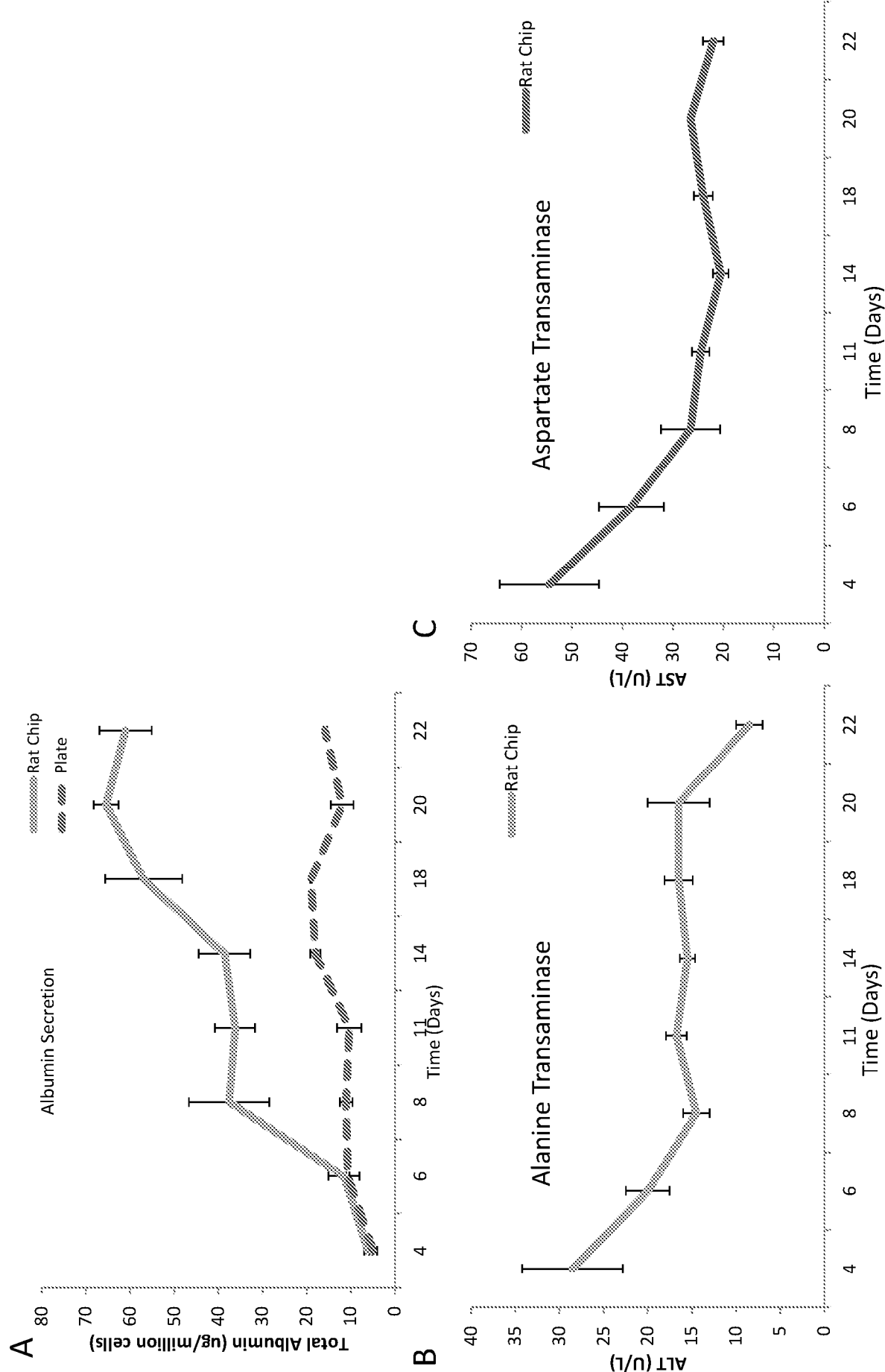
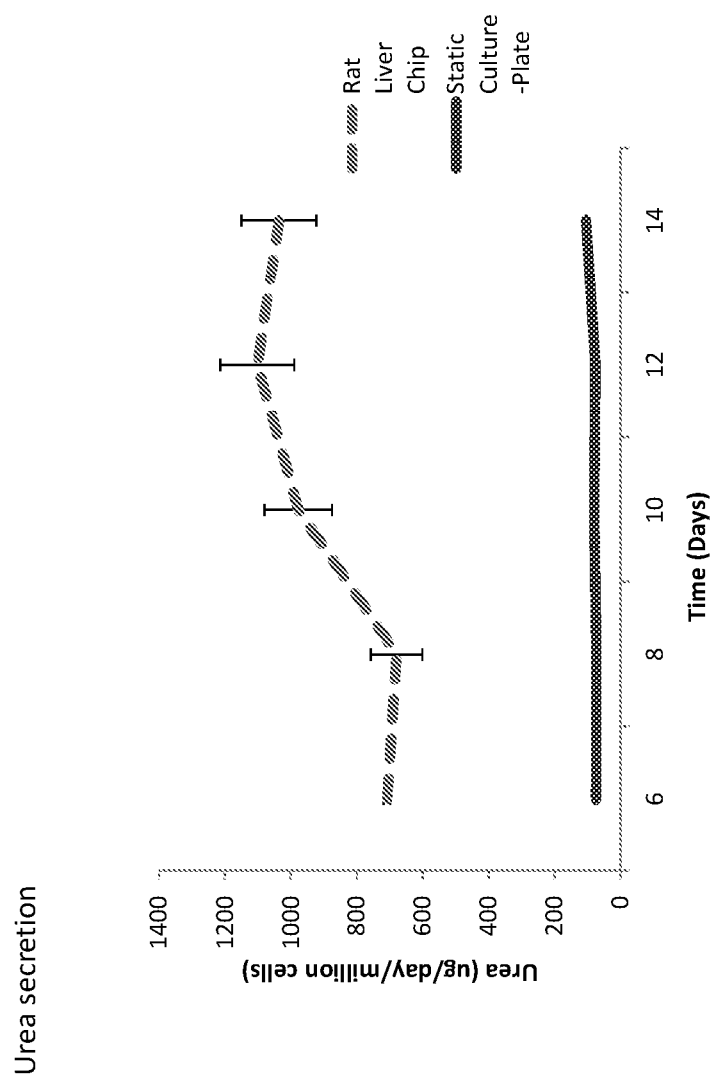
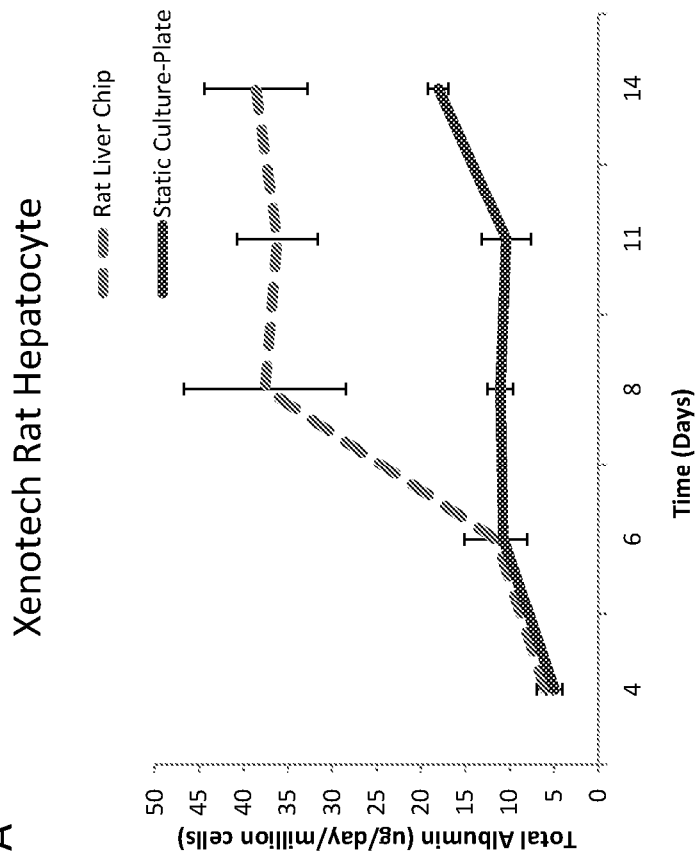


Fig. 22

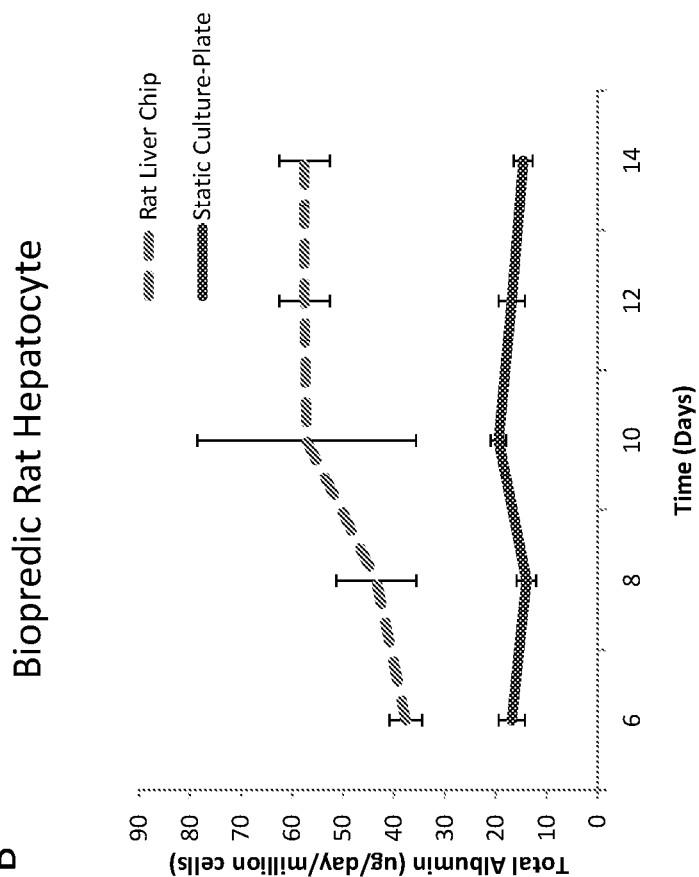


Figs. 23A-23B

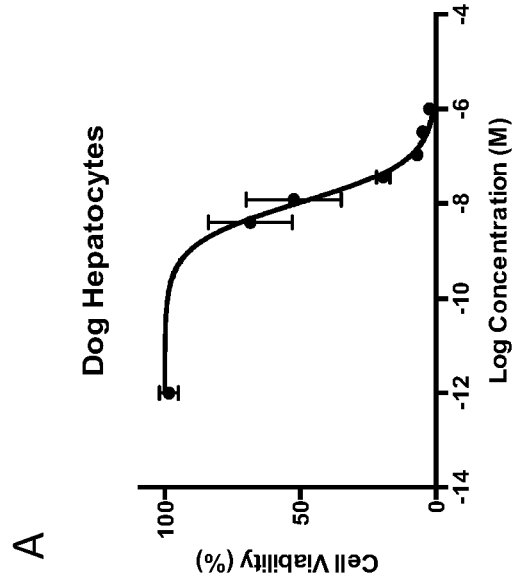
A



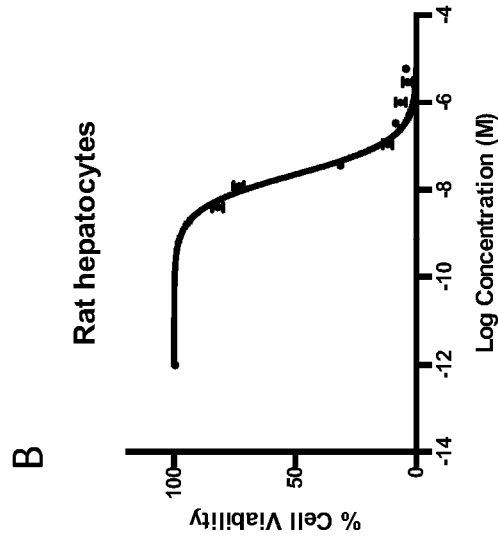
B



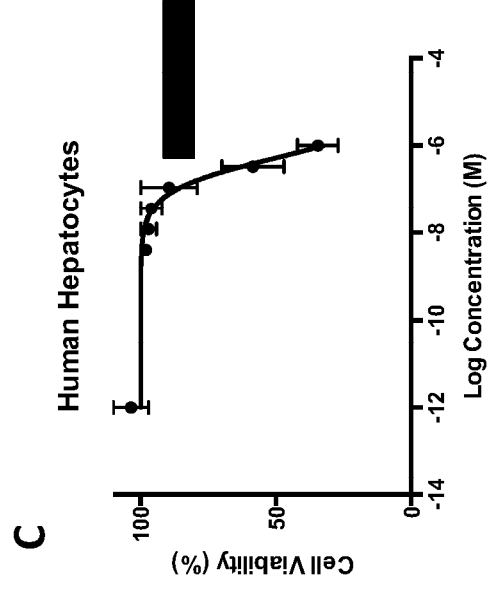
Figs. 24A-24C



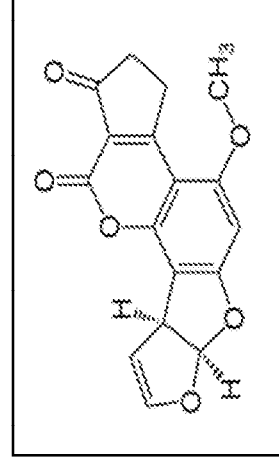
95% CI: 7-16 nM



95% CI: 19-26 nM

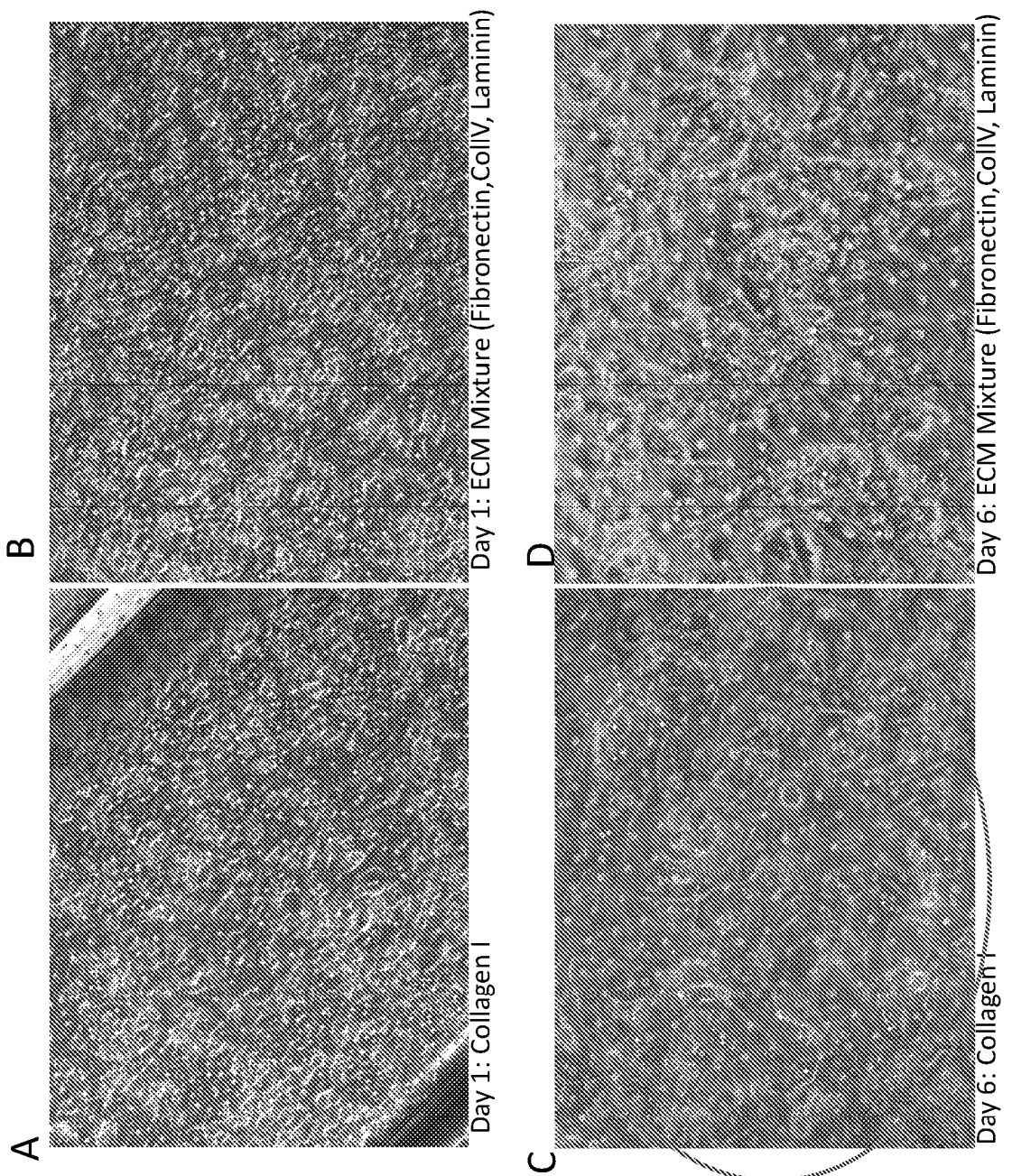


95% CI: 371-733 nM



Aflatoxin

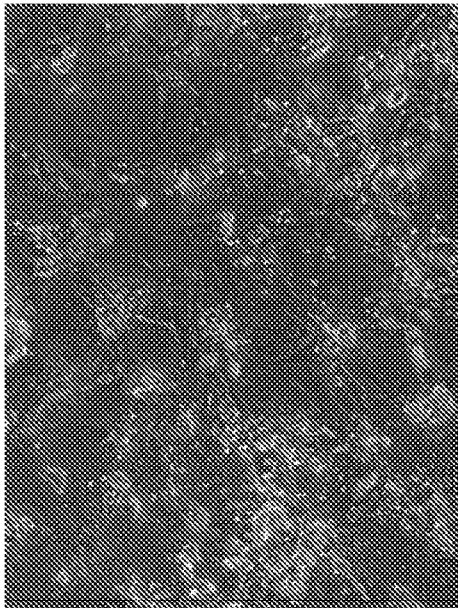
Figs. 25A-25D



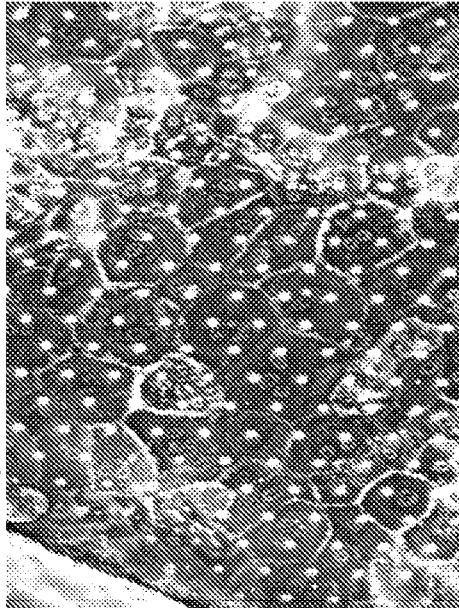
Figs. 26A-26C

A

Static Culture – Plate D14

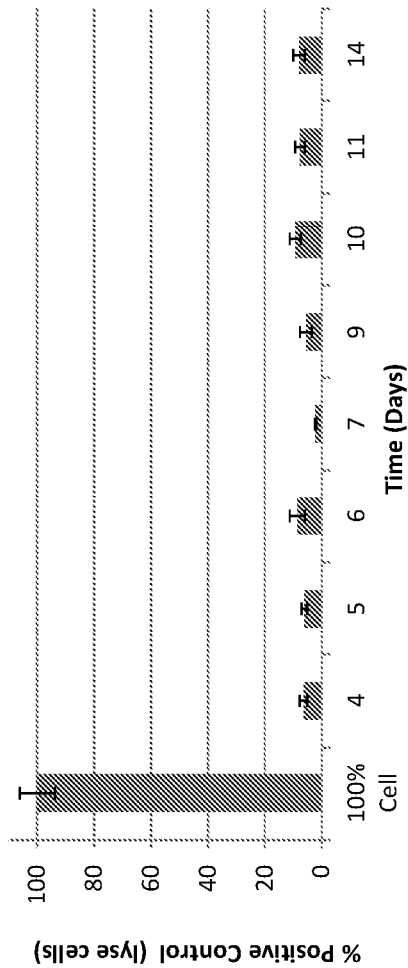


Liver Chip D10



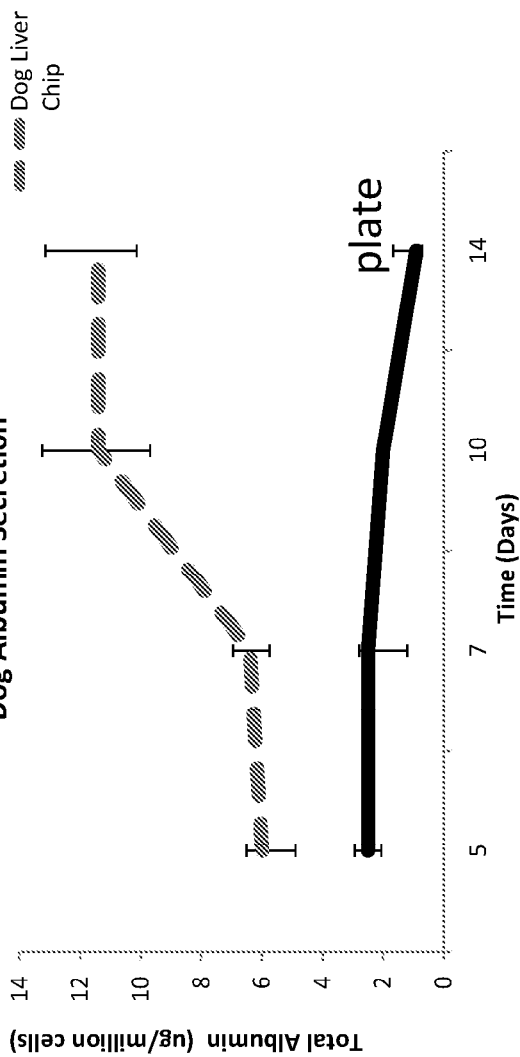
B

LDH Release



C

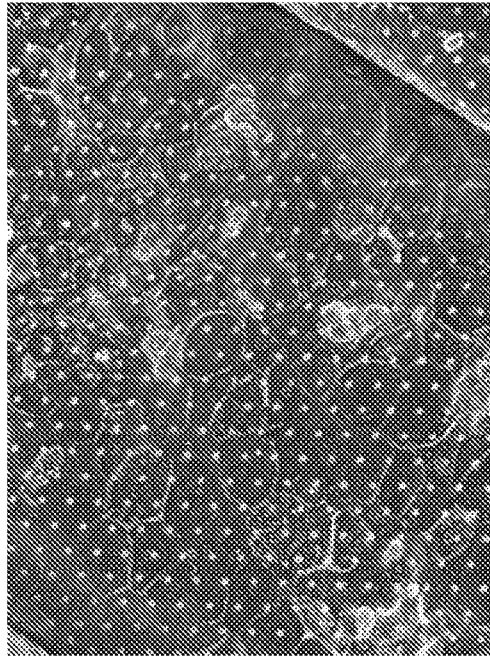
Dog Albumin Secretion



Figs. 27A-27B

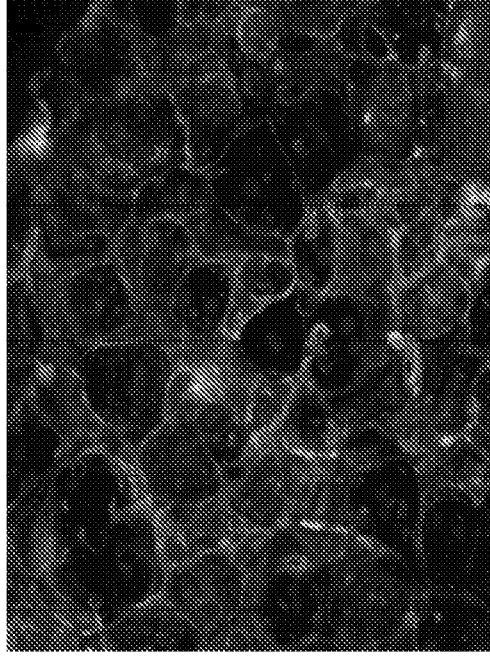
A

Dog Liver Chip D14



B

Dog Liver Chip D14



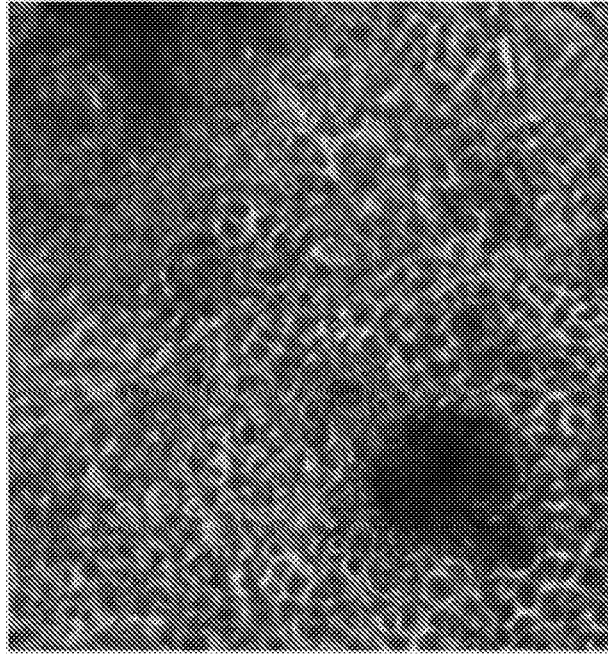
Actin
Nuclei

Figs. 28A-28B

A

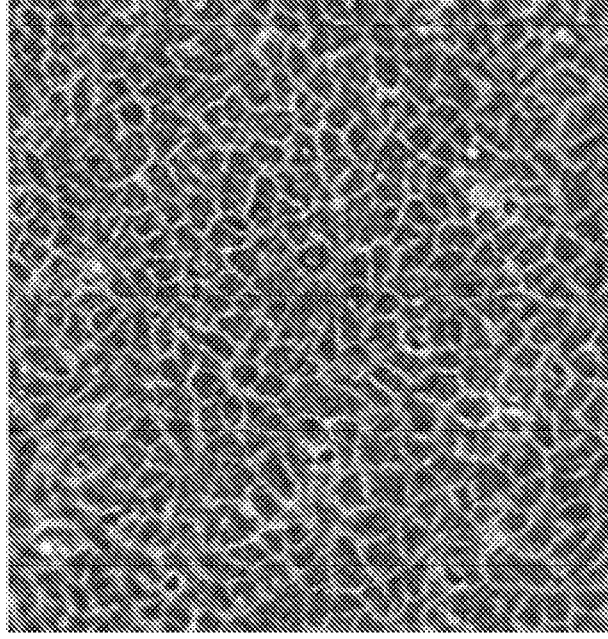
2 weeks of culture

Cells under conventional medium



B

Cells under long-term medium



vs

FIG. 29B

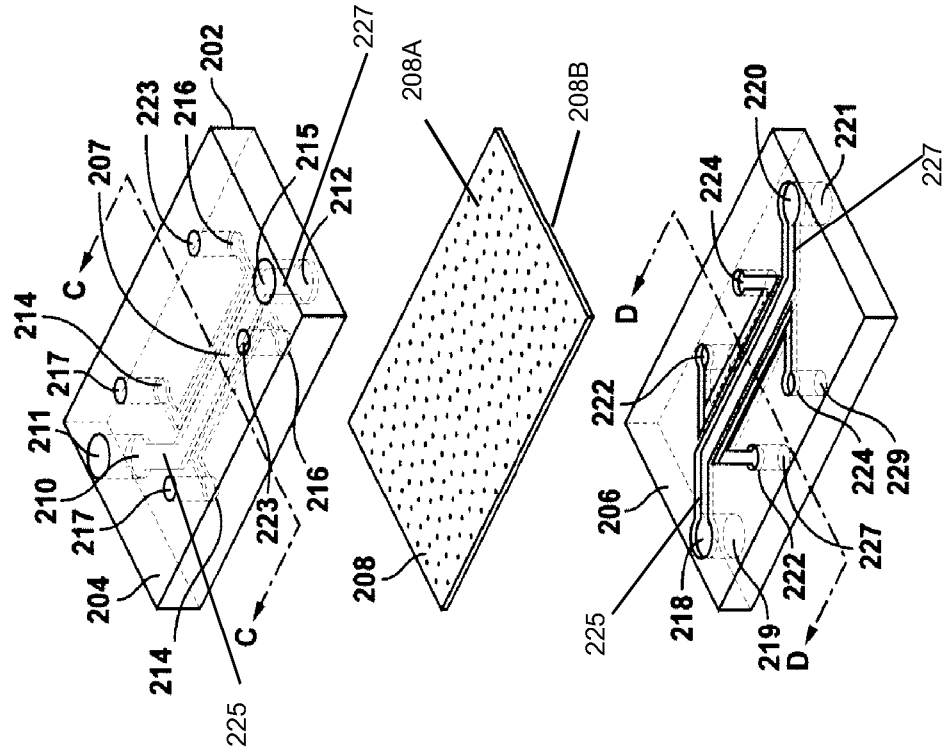


FIG. 29A

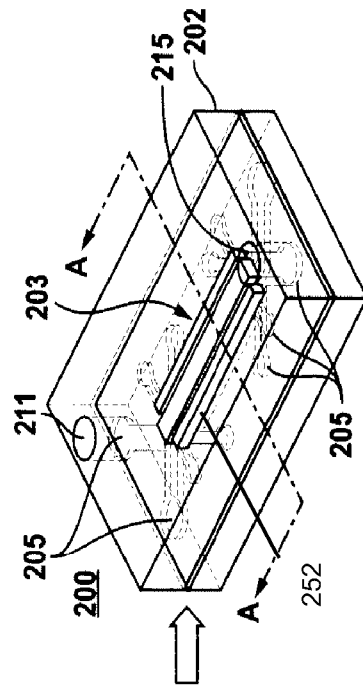


FIG. 30

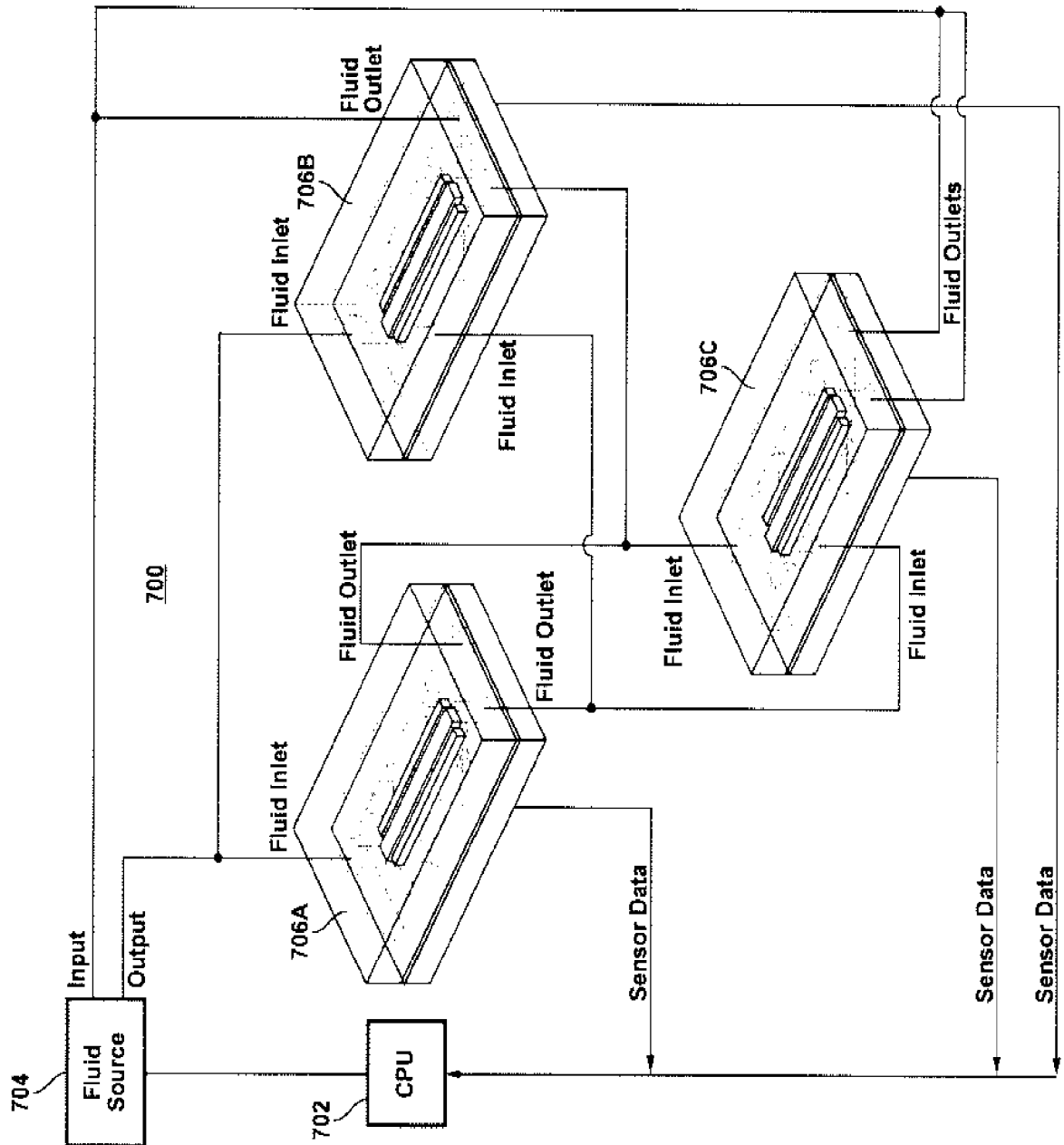
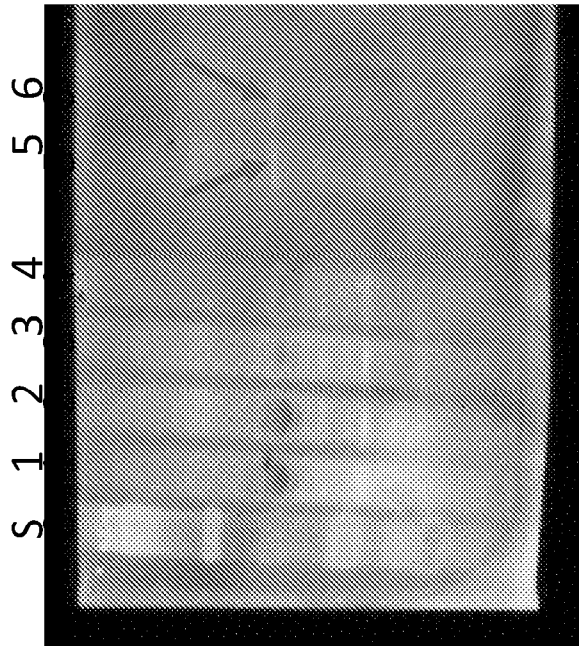


FIG. 31



1. Vehicle Control Nicotine (2-5 μ g)
2. 20 μ M Nicotine (2-5 μ g)
3. Vehicle Control Cisplatin (2-5 μ g)
4. 200 μ M Cisplatin (2-5 μ g)
5. Chip Lysate 1 (8 pg)
6. Chip Lysate 2 (8 pg)

FIG. 32

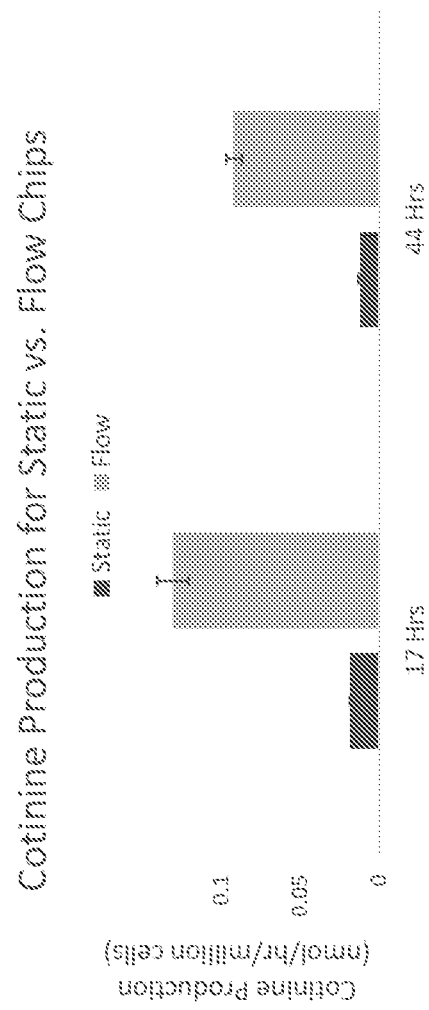


FIG. 33

Cotinine Production for Apical vs. Basal Administration

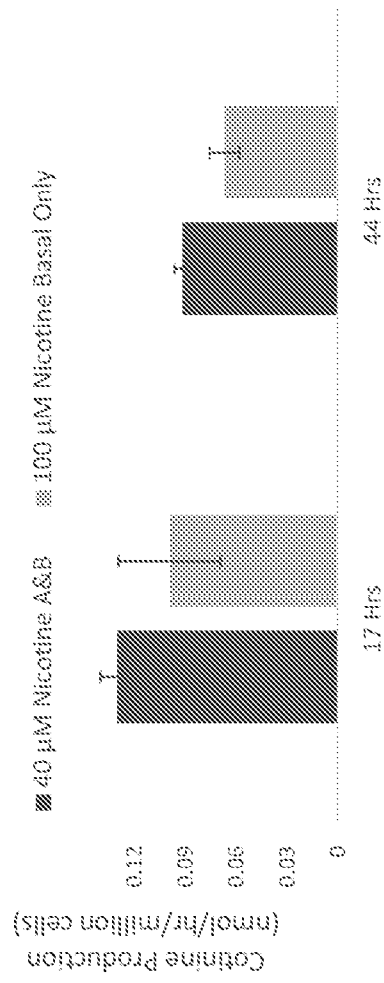


FIG. 34

Cotinine Production for Regular vs. No-FGF LSEC Media

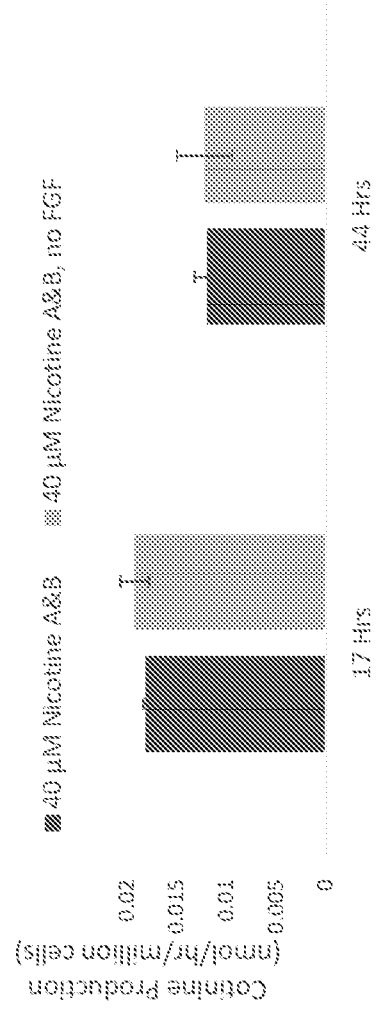


FIG. 35

