Cytological advantages of three-dimensional (3D) culture of human cryopreserved hepatocytes evaluated by comprehensive gene expression.

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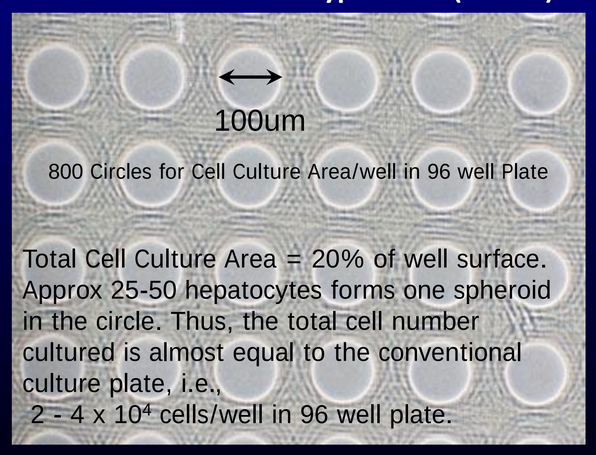
[Purpose] Long-term stability of functioning hepatocytes is desired in drug metabolism and pharmacokinetic (DMPK) study. In this regard, three-dimensional (3D) culture of human hepatocytes has been recognized as a promising DMPK model in vitro. To confirm integrated evaluation of 3D culture, we performed comprehensive gene expression in 3D cultures of primary hepatocytes using Cell-able®, compared with conventional two dimensional (2D) culture.

[Methods] Cryopreserved hepatocytes (Xenotech) were cultured for 14 days by collagen-coat (2D) and Cell-able® (3D) (Transparent). In 3D culture, mouse 3T3 feeder cells were used according to our established protocol. Microarray analysis was done by SurePrint G3 Human GE (Agilent Technologies, Ltd. at Chemicals Evaluation and Research Institute, Japan). Comparison of 3D and 2D culture was examined with relative gene expression of cultured (day14) and thawed (day0) hepatocytes.

【Introduction】

3D cell culture plate used in this experiment

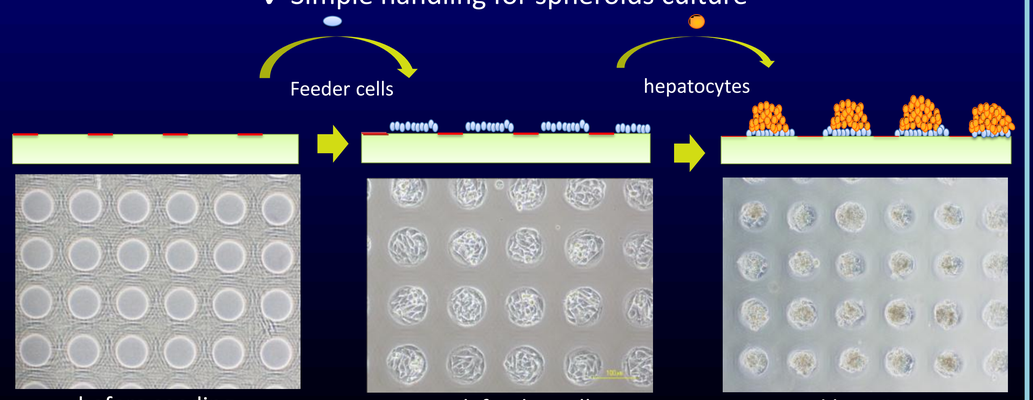
Outline of Cell-able® Hyper view (96well)



Seeding of the cell to Cell-able®

✓Uniform size of spheroids are formed

✓Simple handling for spheroids culture



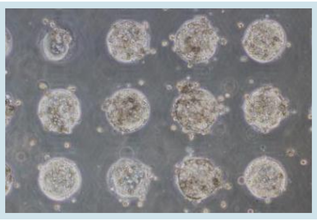
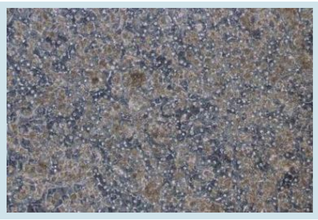
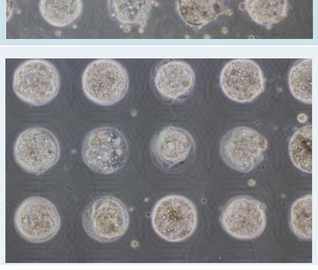
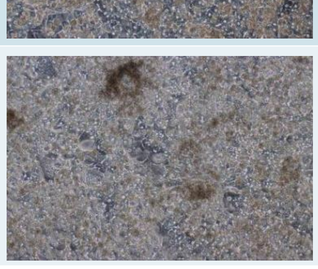
【Materials and Methods】

Experimental condition	
Plate	3D (Cell-able®) 2D (Collagen coat plate)
Culture medium	RM101
Hepatocytes 2 × 10^5 cells/well	HC 1-18 (Xenotech. platable lot.)
Feeder cell 8 × 10^4 cells/well	3T3swiss albino (ATCC CCL-163)
Culture term	14 days
Assay items	Microarray Analysis Photo shot

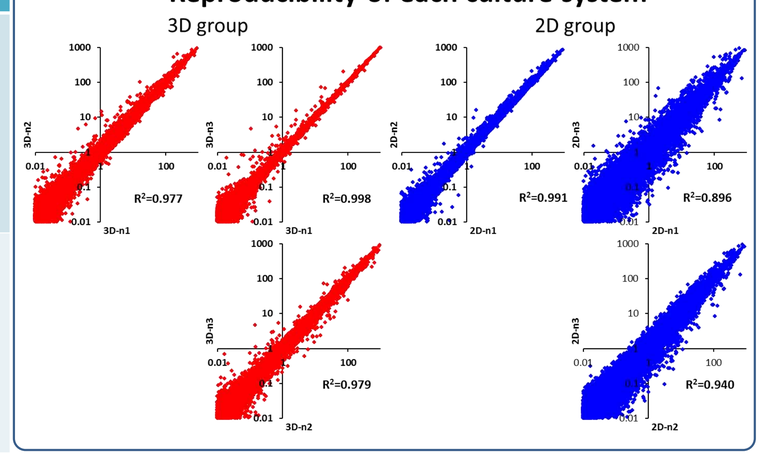
Microarray Sample					
Sample No.	Group Name	Sample Name	Culture term	Culture plate	Feeder cells
1	d0	d0	0 day	-	-
2	3D group	3D-n1	14 days	Cell-able®	3T3swiss albino
3		3D-n2			
4		3D-n3			
5	2D group	2D-n1		Collagen coat plate	-
6		2D-n2			
7		2D-n3			

【Result】

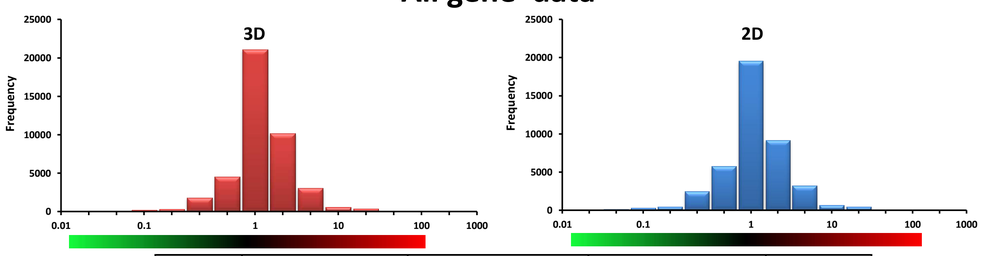
2D and 3D observation

	3D	2D
day7		
day14		

Reproducibility of each culture system

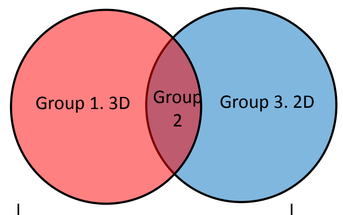


All gene data



	Threshold value (Revelation ratio)	2-fold over or 0.5-fold Following	5-fold over or 0.2-fold Following	total
3D / d0	up-regulation	2300	506	2806
	down-regulation	3526	578	4104
2D / d0	up-regulation	2741	531	3272
	down-regulation	4556	758	5314

Venn diagram of Change gene group



Group 1	Group 2	Group 3
Influence of 3D culture and feeder cells	Influence of Freeze-thaw operation and culture medium	Influence of 2D culture

List of Switch ON type gene

group − 1			
ABCB9	FGF5	NHS	VWA3B
ADAM23	FLNC	NKAIN2	WISP1
ADAMTSL1	FOXG1	NKAIN4	WNT3A
AFF2	FOXP3	NOVA1	ZBTB12
AGPAT4	GATA3	NRG2	ZNF521
ANGPTL7	GATS	ODF4	ZNF674
ARHGAP28	GDAP1L1	ODZ4	
ARHGEF25	GDF1	OR3A4P	
BCL11B	GIT1	OR4M1	
BCL2	GLI3	OSTN	
BEND5	GPM6B	P4HA3	
BNC2	GPR156	PADI1	
BTBD9	GPR45	PAK3	
BUB1	GRIA3	PAQR7	
C14orf48	GRIK1-AS1	PCDH7	
C7orf52	HIST3H2A	PDE7A	
CACNA1A	HKDC1	PENK	
CACNA2D1	HOXA2	PI15	
CACNG7	HOXD8	PKNOX2	
CAV3	HOXD9	PLK1	
CCDC85A	HS6ST2	PLXNA4	
CD248	IGF2BP2	PODXL2	
CD34	IRX1	POTED	
CD3E	IRX2	PRAMEF10	
CDH11	IRX5	PRDM5	
CDK1	KIF20A	RFC3	
CDR2L	KIF23	RGMA	
CEL	KIF26B	ROR2	
CELF2	KITLG	ROS1	
CELF4	KRT14	SHOX2	
CITED1	KRTAP10-6	SIX4	
COL5A1	KRTAP21-1	SLC22A15	
CPEB1	LEF1	SLC32A1	
CSF1	LINC00239	SLC6A6	
CSHL1	LIPI	SLC6A8	
CXCL12	LMTK3	SNAR-E	
CXCR3	LOXL3	SORCS1	
DCLK1	LRRTM4	SPEG	
DDX26B	MAP3K12	SPTB	
DLK1	MATN4	SRGAP3	
DMRTA2	MED20	TAGLN3	
DUSP7	MFAP2	TCL1A	
DYNC2H1	MGAT3	TFAP2A	
EBF1	MGC50722	TMEM164	
EML1	MS4A10	TNMD	
EMX2	MYBPHL	TNNI2	
ENAH	MYH6	TRERF1	
ERC2	MYL2	TRIM3	
FAM59B	NEB	TRPV5	
FAM5C	NETO2	TWIST1	

group − 2				
AACS	DCX	LAMA3	RAB27B	ULBP2
ABLIM2	DDIT4L	LAMC2	RAB3B	UTS2
AHNAK2	DIRAS2	LIPH	RALGPS1	VLDLR
AIM1L	DLK2	LOX	RBM24	VSIG10L
ANKRD1	DMBT1	LPCAT1	REG1A	VTCN1
AP1M2	DTNA	LRP8	REG1B	WLS
APLN	DYNC1I1	LYPD1	RGS4	WSCD1
ARHGAP22	ECEL1	LYPD6	RHOQ	ZWINT
ARHGEF2	EDA2R	MAP1B	RIMBP3	
ASPHD2	EEF1A2	MAP7D3	RIMKLA	
ASXL2	EGLN3	MAPK12	RNF213	
ATP2B4	EGOT	MAPT	RNFT2	
BCAS1	ELFN2	MELK	SBK1	
BCAT1	EPB41L1	MFI2	SCN1B	
BMP8B	FAM155B	MFI2	SCN3B	
C11orf80	FAM189A2	MGAM	SCTR	
C12orf39	FGF1	MICAL1	SEMA4F	
C12orf75	FMNL2	MTL5	SEPT5	
C1orf116	FP588	MYOF	SFTA2	
C1QL1	GAL	NANOS1	SHISA9	
C20orf118	GCNT3	NCF2	SLC4A3	
C3orf52	GLIPR1	NEBL	SLC6A10P	
C8orf48	GPR37L1	NPPB	SLC7A11	
C8orf84	GPR64	NPTX2	SLMO1	
CA12	GPRIN1	NQO1	SNORA12	
CA9	GPRIN2	NXPH4	SPC25	
CABYR	GPSM2	OSBPL3	SPINT1	
CALB2	GRAMD1A	OXCT2	SPOCD1	
CAMP	GXYLT2	OXTR	SPOCK1	
CAMSAP1	HAS3	PAGE4	SPRR1A	
CAMTA1	HELLS	PAQR4	SRSF12	
CAPN6	HES2	PCSK5	STK39	
CBR3	HS1BP3	PIK3CD	SULT2B1	
CCDC109B	HS1BP3	PIP5KL1	SYT13	
CCDC165	IL17D	PLCD3	TEX11	
CCDC80	IQCA1	PLEKHN1	TGFB2	
CD163L1	ITGA3	PLXNC1	THBS2	
CDC42BPG	KCNJ11	PPP4R4	TMC5	
CDCA2	KCNJ6	PRAMEF4	TMEM119	
CDH13	KIAA1244	PRAMEF8	TMEM136	
CDH6	KIAA1324	PRRX1	TMEM156	
CDS1	KIAA1549	PRSS1	TMEM217	
COCH	KIAA1841	PRSS16	TMEM61	
COL15A1	KIF3C	PRSS56	TNC	
CRCT1	KIF5C	PRTFDC1	TNFAIP6	
CREB5	KLC2	PSG8	TRIM7	
CTHRC1	KLC3	PSORS1C1	TSPAN5	
CXCL6	KLHDC7B	PTGFR	TTC39A	
DAGLA	KRT23	PTX3	TUB	
DAPK2	KRT80	RAB25	TUBAL3	

group − 3				
ABCC1	CXCL10	KLRC4	PPP1R9A	TSPO2
ABCC4	CYP24A1	KRT17	PPP2R2C	TTTY15
ACCN2	DEFB103B	KRT6A	RAB42	TUBB2B
ACTA1	DGCR14	LAMP3	RAB6B	UAP1L1
ADAM21	DGKG	LBH	RASGRF2	UBASH3B
ADAM9	DIAPH3	LINC00239	RASGRP1	UBE2C
ADORA2B	DIRAS1	LMTK3	REEP2	ULBP1
AFAP1	DKK1	LPAR2	REG3A	UNC119B
ALDH3A1	DPCR1	LYL1	RHBDL2	UPK1B
AMPD3	DPYSL4	MAP6	RIMS3	USH1C
AMZ1	DUOX1	MAP7D2	RIPK3	UTS2D
ANKRD13B	DUOXA2	MB	ROR1	VGF
ANKRD2	DUSP13	MCTP1	RTN1	VPS53
ARG2	E2F1	MKL1	S100A3	WDR78
ARL14	EGFL6	MLLT3	SAMD9	XKR3
ATP2C2	ELOVL7	MMP10	SAMD9L	ZFP57
B3GNT4	ENO2	MNX1	SCGB1D2	ZNF215
BEST1	ENPP5	MPO	SEMA3C	ZNF850
BHLHE41	EREG	MPPED2	SEMA7A	
BICC1	FABP3	MRAP2	SGPP2	
BRSK2	FAM150A	MSC	SH3D21	
C11orf86	FAM169B	MTL5	SHCBP1	
C15orf27	FAM54A	MUC13	SIX1	
C17orf69	FAM59B	MUCL1	SLC34A2	
C1orf106	FANCD2	MYO7B	SLC35F3	
C21orf7	FBXL2	MYZAP	SLC4A11	
C3orf64	FGF2	NAV3	SLC6A8	
C6orf105	FIGNL1	NCS1	SLC7A6	
CAPN13	FLJ43315	NEK11	SLITRK4	
CAPN13	FLRT2	NETO2	SP6	
CCDC103	FOXL1	NPAS1	SPECC1	
CCDC112	GALNT12	NRCAM	STC2	
CCL26	GJB3	NRIP3	STK17B	
CCNO	GJB4	NRSN2	STK33	
CDCP1	GOLGA7B	OBFC1	STXBP1	
CDKN2A	GPR68	ORAI2	SULT1C3	
CDKN3	GPX8	ORC6	TC2N	
CEACAM6	GTSE1	OXCT1	TMEM63C	
CEACAM7	HAVCR1	P2RX5	TMPRSS3	
CENPE	HKDC1	PAPPA	TNFRSF11A	
CENPM	IGSF1	PBK	TNFRSF9	
CEP19	IGSF3	PCDHA11	TNNT1	
CEP55	ITGA2	PEG10	TNS4	
CERS1	ITGB6	PHEX	TREM1	
CHEK1	ITGB8	PHGR1	TRIM31	
CHRNA7	KCNK13	PKP3	TRIM36	
CKMT1A	KIAA0408	PLEKHG4	TRIM59	
CNIH3	KIF1A	PNMA2	TRPV6	
CPA4	KIF1B	PNMAL1	TSGA10	
CST6	KLRC1	POPDC3	TSPAN15	

List of Switch OFF type gene

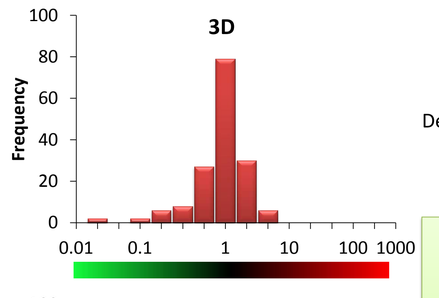
group − 1										
ACOXL	LOC729324	ABCA13	CCDC27	EPHB1	IL10	NLRP3	SIGLEC14	ACSM2A	FAM53B	LOC645434
ARID5A	MEI1	ACOT6	CCL19	ERVI−1	IL4R	NMUR1	SIGLEC7	ADRA1A	FCN1	LOC646976
ASCL2	MPEG1	ACSS1	CCL21	ESR1	INMT	NPY1R	SKOR2	ADRA2B	FCRL2	LOC728095
ATP10D	NAALADL2	ADAMTS16	CCL4	F13A1	IRGM	NR4A3	SLC10A7	ARHGAP29	FLT1	LPA
BCL2A1	NTRK2	ADARB2	CCNDBP1	FAM107A	JAM2	OR2D3	SLC34A1	ASGR1	FMO2	LRAT
C14orf180	NUP62CL	ADCY10	CD209	FAM190A	KIAA1751	OR8K1	SLC7A8	ASPN	FOLR2	LUC7L3
C22orf24	NUPL1	AFF1	CD209	FAM19A4	KIF19	OXR1	SLC8A1	AZGP1P1	GDF10	MAMDC2
C2orf40	PARM1	AGER	CD300A	FAM71A	KIF20B	PARP1	SLITRK3	BCOR	GDPD4	MASP1
CCR7	PAX9	ALLC	CD33	FAM9B	KRT40	PBLD	SMG7	BHLHE22	GIMAP6	MCART6
CD37	PI16	ALS2CR11	CD5L	FCGR2B	LGI1	PDZRN4	SNORA16B	BRD7	GOLGA6A	MERTK
CD53	PLIN1	ANKRD20A	CD69	FCGR2C	LHX6	PHLDB3	SNORD8	C16orf54	GPLD1	METTL20
CNTNAP3	PNMT	ANKRD55	CDH19	FCN2	LILRA6	PLAC8	SPDYE5	C17orf67	GPR116	MUC2
CXCL14	PRUNE2	ANO1	CETP	FCRL5	LILRB1	PLCB2	SPRY3	C20orf160	GPR32	MYCN
CXCL3	PTGS2	AQP6	CHRDL1	FGL2	LILRB2	POTEE	SSTR2	C20orf62	HBA2	MYH7B
CXCL9	PTPRC	ARGLU1	CLEC4G	FNDC3A	LINC00161	POU2AF1	ST6GALNA	C4orf11	HEPACAM	MYO16
CYBB	RAPGEFL1	ARHGAP15	CLEC4M	FOXP2	LINC00324	PPP2R1B	STAB2	C6orf124	HEPN1	NECAB2
CYTH4	REXO1L1	ARHGEF7	CLSTN2	FRZB	LOC644145	PRDM1	STEAP4	C9orf47	HIST1H3H	NGFR
DERL3	RFX3	ARNTL	CMAHP	GALP	LOC646851	PRKAR2B	SULT6B1	CCDC144A	HLA-DQB1	NOL4
DNAH14	RIPPLY1	ASB4	CMKLR1	GAPVD1	LPPR4	PRY2	SYNPO2	CCDC73	HNF1A	NPEPPS
FAM117B	RNASE6	ATP8A2	COL11A2	GDF2	LRRC39	PTPRVP	TCP1	CCNC	HNRNPK	NS3BP
FAM26F	RUNX3	ATXN2	COLEC10	GHRL	LRRC70	PVALB	TIMD4	CDH18	HORMAD2	NTRK3
FBXL21	SAMD12	AVIL	CSF3	GM140	LST1	RABGAP1	TIPARP	CEACAM22	HOXA6	NYNRIN
FCGR1B	SAMSN1	BAALC	CTNNA3	GNN	LYPD4	RALGPS2	TJP2	CH25H	HSD17B3	OGN
FOSB	SDPR	BMP5	CUBN	GOLGA7B	LYVE1	RBM44	TNF	CHRNA4	HSPA12B	OIT3
GATA5	SEMA3G	BPI	CXorf61	GPM6A	MACROD2	RBM44	TNFAIP8L2	CHTOP	IDO2	OR10G8
GGTA1P	SFRP1	BTNL9	CYP26A1	GPR182	MAN1B1	RFPL1	TPSAB1	COLQ	IMMT	OR6Q1
GLT8D2	SH2D1A	C10orf71	CYP4Z1	GZMK	MBD2	RGS1	TPSD1	COPG2IT1	INS-IGF2	PARVG
GPR65	SNORA33	C15orf2	DACH1	HAAO	MEGF11	RGS18	TSPAN32	CXCL13	JAKMIP2	PCDH11X
HAND2	SYCE2	C17orf87	DBH	HAS1	MGC12488	RNU12	TTC9C	CYYR1	KAZALD1	PCDH20
HLA-DRA	TAF7L	C1QC	DCDC2B	HBA2	MIR17HG	RPS16P5	TTL	DKFZP586E	KCNJ3	PDE4B
HLA-DRB5	TMC8	C1QTNF9	DCST1	HBB	MRO	RSPO3	TUBE1	DNAH6	KCNMA1	PDE7B
ICAM4	TMEM154	C20orf112	DEFA3	HDC	MS4A6A	S100A12	UTY	DPRXP4	KLF12	PDPR
IGLL5	TMEM179	C21orf104	DEFA9P	HEMK1	MUC12	S100A8	UXT	DSG1	KLHDC1	PFN3
IL13RA2	TMEM211	C2orf73	DIP2C	HGF	MYL10	SCARA5	WDR86	EBF1	KLHL14	PODN
IL1B	TSPAN11	C6orf58	DISP2	HIST1H4A	MYL3	SCN7A	WWC2	ECM2	LDB2	POU6F2
ITLN2	TSPYL2	C6orf81	DLX1	HIST2H2BF	MYO15A	SCN8A	XCL1	EVI2B	LGSN	PRO2852
IVNS1ABP	TXNL1	C8orf39	DNAI1	HLA-DOA	MZB1	SDK1	ZCCHC11	EVX2	LILRB5	PRODH
KIAA1875	UPP2	C9orf135	DOC2A	HLA-DQA1	N4BP2L1	SEC14L3	ZCCHC6	EXOC3L2	LINC00476	PRSS50
LILRB3	UST	CBLN4	EBI3	HLA-DQB1	NBLA00301	SELE	ZNF507	F10	LINC00477	PTH1R
LILRB5	VCAM1	CBR1	EDNRB	HSPA8	NEK10	SELP	ZNF735	FAM166A	LOC339240	PTN
LOC401845	WDR66	CCDC152	EGFLAM	HSPA8	NLGN4X	SETD3		FAM184A	LOC401845	PTPRB

group − 2												
LOC645434	RAD51AP2	ZNF295										
LOC646976	RAMP3											
LOC728095	RANBP3L											
LPA	RBM14											
LRAT	RCL1											
LUC7L3	RND2											
MAMDC2	RNU4ATAC											
MASP1	RPS15AP10											
MCART6	RUFY2											
MERTK	SCAPER											
METTL20	SHC2											
MUC2	SLC10A5											
MYCN	SLC16A10											
MYH7B	SLC1A2											
MYO16	SLC25A27											
NECAB2	SLC2A3											
NGFR	SOX13											
NOL4	SPATA13											
NPEPPS	SPON1											
NS3BP	STAB1											
NTRK3	STRC											
NYNRIN	SUCNR1											
OGN	SYNRG											
OIT3	SYT9											
OR10G8	TAS2R30											
OR6Q1	TBX6											
PARVG	TCTE3											
PCDH11X	TIAL1											
PCDH20	TIE1											
PDE4B	TMED6											
PDE7B	TNFRSF6B											
PDPR	TNN											
PFN3	TRAF3IP3											
PODN	TRIP12											
POU6F2	TRPV1											
PRO2852	TSPY2											
PRODH	UST											
PRSS50	UTP23											
PTH1R	VAV3											
PTN	WDR33											
PTPRB	WISP2											

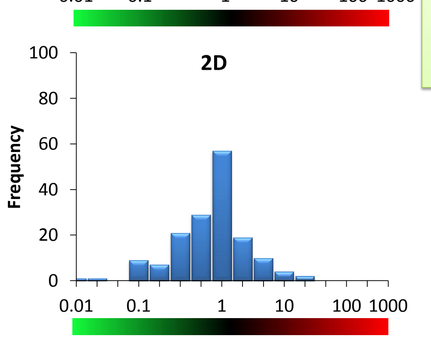
Switch ON type ; The gene which was Not Detected flag in d0 and Detect or Compromised flag in 3D group or 2D group .
Switch OFF type ; The gene which was Not Detected flag in 3D group or 2D group and Detect or Compromised flag in d0.

DMPK-related genes

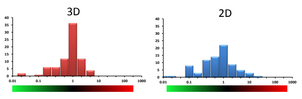
Whole data of the DMPK-related genes



Details

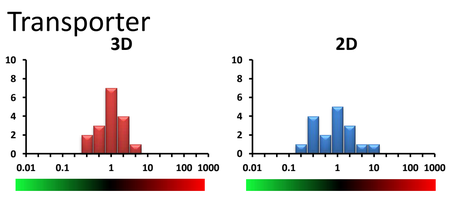


CYPs



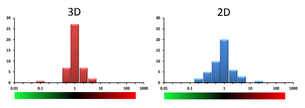
	down-regulated gene 0.2-fold >	down-regulated gene 0.5-fold >	no change	up-regulated gene 2-fold <	up-regulated gene 5-fold <
3D	CYP26A1	CYP2C19 CYP4F11	CYP11A1 CYP26B1 CYP2R1 CYP4V2	CYP4F22	
	CYP2C8	CYP2C9 CYP4Z1	CYP11B1 CYP26C1 CYP2S1 CYP4Z2P	CYP27C1	
	CYP2E1	CYP2D6	CYP17A1 CYP27A1 CYP2U1 CYP51A1	CYP7A1	
	CYP3A43	CYP2G1P	CYP19A1 CYP27B1 CYP2U1 CYP7B1		
	CYP3A5	CYP2J2	CYP1A1 CYP2A13 CYP2W1 CYP8B1		
	CYP4A11	CYP39A1	CYP1B1 CYP2A7 CYP46A1		
	CYP4A22	CYP3A4	CYP1B1-A CYP2B6 CYP4F11		
	CYP4B1	CYP3A5	CYP20A1 CYP2C18 CYP4F12		
	CYP4X1	CYP3A7	CYP21A2 CYP2F1 CYP4F2		
	CYP4Z1	CYP4F30P	CYP24A1 CYP2G1P CYP4F3		
	10	12	35	3	0
2D	CYP2E1 CYP3A7	CYP17A1 CYP3A5	CYP11A1 CYP27C1 CYP4F30P	CYP21A2	CYP2S1
	CYP26A1 CYP4A11	CYP19A1 CYP46A1	CYP11B1 CYP2C18 CYP4Z2P	CYP19A1	CYP19A1
	CYP2A13 CYP4A11	CYP26B1 CYP4F2	CYP11B2 CYP2F1 CYP51A1	CYP1A1	CYP24A1
	CYP2A7 CYP4A22	CYP27A1 CYP4F3	CYP19A1 CYP2G1P CYP7A1	CYP27B1	
	CYP2C19 CYP4B1	CYP2B6 CYP4F30P	CYP1A2 CYP2R1 CYP7B1	CYP2S1	
	CYP2C8 CYP4Z1	CYP2G1P CYP4F8	CYP1B1 CYP2U1 CYP8B1		
	CYP2C9 CYP4Z1	CYP3J2 CYP4V2	CYP1B1-A CYP3A7		
	CYP2D6	CYP2W1 CYP4X1	CYP20A1 CYP4F11		
	CYP3A43	CYP39A1	CYP21A2 CYP4F12		
	CYP3A5	CYP3A4	CYP26C1 CYP4F22		
	17	18	26	5	3

Transporter



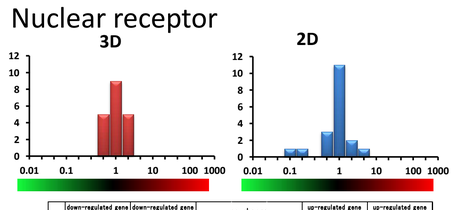
	down-regulated gene 0.2-fold >	down-regulated gene 0.5-fold >	no change	up-regulated gene 2-fold <	up-regulated gene 5-fold <
3D		SLCO1A2	ABCB11 SLCO1A2	ABCC1	
		SLCO1B1	SLCO1A2 SLC22A4	SLC22A2	
		SLC22A6	ABCC3 SLC22A5		
		SLC10A1	ABCB11 SLC22A7		
		SLC22A1	ABCC2		
	1	5	9	2	0
2D	SLC10A1	SLCO1A2 ABCB11	ABCC2	ABCB1	ABCC1
	SLC22A1	SLCO2A1 SLCO1B1	ABCC3	SLC22A4	
		SLCO2A1 SLC22A7	SLC22A2	SLC22A5	
		SLC22A7 SLC22A6	SLCO2B1		
		SLCO2B1			
	2	9	4	3	1

Conjugation



	down-regulated gene 0.2-fold >	down-regulated gene 0.5-fold >	no change	up-regulated gene 2-fold <	up-regulated gene 5-fold <
3D		GSTA7P	GSTA2 GSTA3 GSTO2 GST2B10	UGT3A2	
		GSTA5	GSTA4 GSTP1 GST2B11		
		GSTM4	GSTCD GSTT1 GST2B15		
		GSTTP2	GSTK1 GSTT2 GST2B4		
		UGT2A2	GSTM1 GST2B GST3A1		
		UGT2B7	GSTM2 GSTTP1 UGT8		
			GSTM2P1 GST1A6		
			GSTM3 GST1A8		
			GSTM5 GST2A1		
			GSTO1 GST2A3		
	1	6	26	1	0
2D	GSTA2	GSTM4	GSTA3 GSTT2B		UGT3A2
	GSTA7P	GSTA5	GSTA4 GSTTP1		
	GSTM2P1	GSTM1	GSTCD GST1A6		
		GSTM2	GSTK1 GST1A8		
		GSTM5	GSTM2 GST2A1		
		GSTTP2	GSTM3 GST2A3		
		UGT2A2	GSTO1 GST2B11		
		UGT2B10	GSTO2 GST2B4		
		UGT2B15	GSTT1 GST3A1		
		UGT2B7	GSTT2 UGT8		
	3	10	20	0	1

Nuclear receptor



	down-regulated gene 0.2-fold >	down-regulated gene 0.5-fold >	no change	up-regulated gene 2-fold <	up-regulated gene 5-fold <
3D			CAR AHR PXR VDR		
			HNF4a AHRR GR		
			RXRG HNF4g RXRa		
			AHR LXRa RXRb		
			FXR RXRg		
	0	4	11	0	0
2D	CAR	AHR	AHRR GR	VDR	
		RXRG	HNF4a RXRa		
		AHR	HNF4g RXRb		
			FXR RXRg		
			PXR		
	1	3	9	1	0

【Results and Discussion】

Inter-well deviation of gene expression was smaller in 3D than 2D culture. It suggests that the uniform culture circumstance of Cell-able®. Judging from gene expression ratios (day14/day0), numbers of genes with increased expression were 2306 in 3D and 3272 in 2D, and those with decreased expression 4104 in 3D and 5314 in 2D. The results indicated that 3D culture maintained original cellular characteristics better than 2D even after 14 days culture. The tendency was also observed with DMPK-related genes such as CYPs, nuclear receptors, and transporters.

【Conclusion】

Cell-able®, a microfabricated cell array system for 3D culture maintains original hepatocyte characteristics in terms of gene expression. Still more detailed analysis is due to be conducted focusing on an adhesion factor from now on.

【Acknowledgment】

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