

JPET #252940

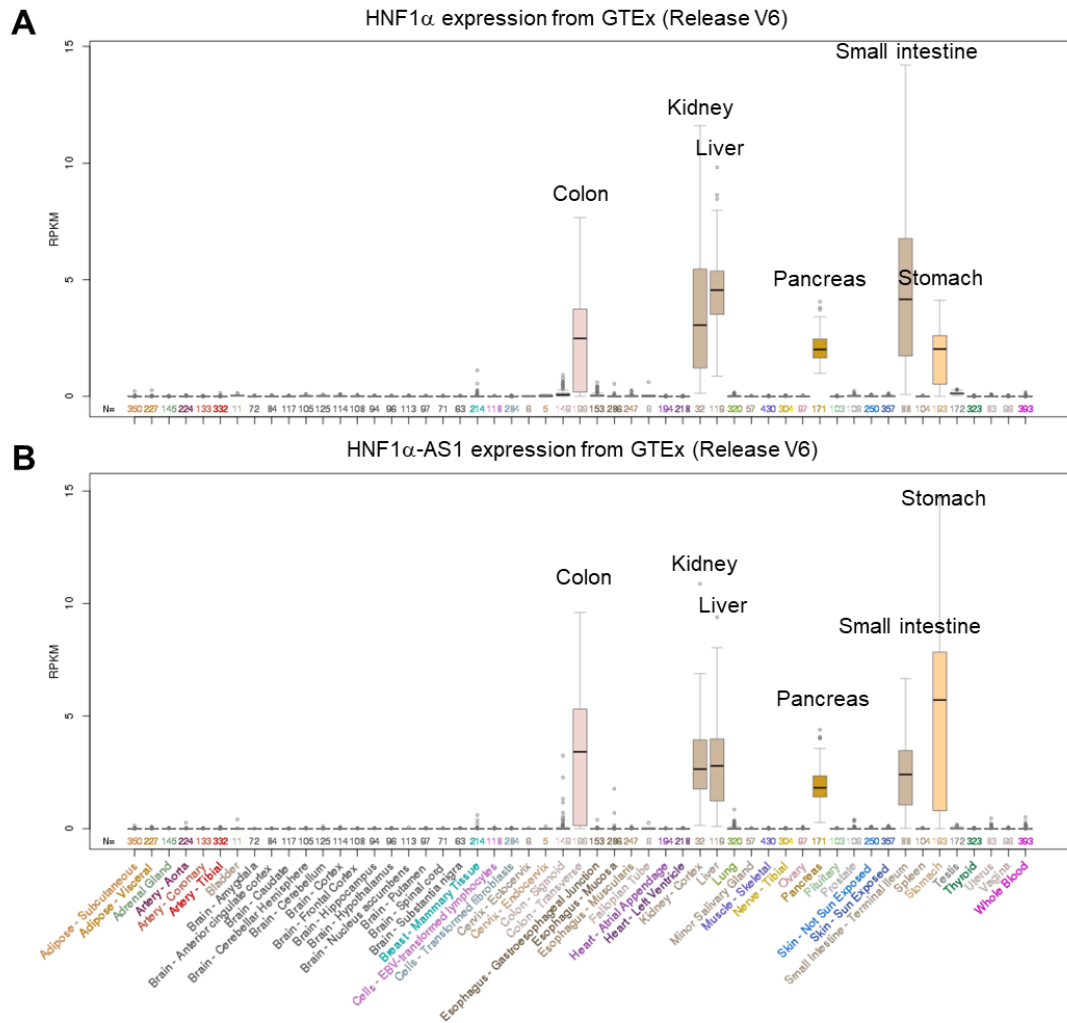
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The HNF1 $\alpha$ -regulated lncRNA HNF1 $\alpha$ -AS1 is Involved in the Regulation of Cytochrome P450 Expression in Human Liver Tissues and Huh7 Cells

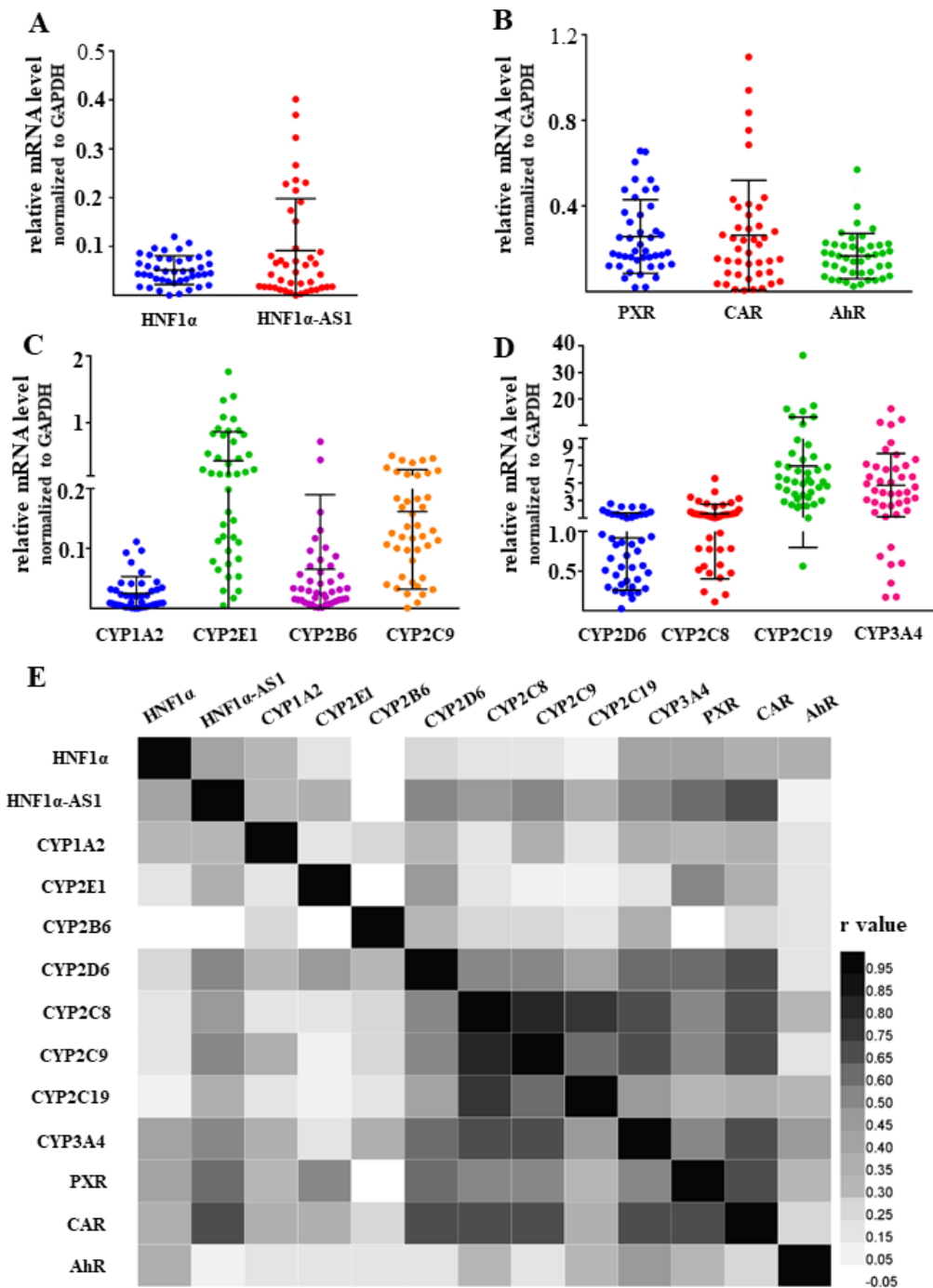
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**Supplemental Table S1. Primers for RT-qPCR**

Gene	Forward primer	Reverse primer
CYP1A2	GGTGGAGGTAGGAGCAACAC	CTAGCAGGGACAAACAGCCT
CYP2E1	TTCTCCTAGGGCACAGTCGT	AGGGAAGGTACTGCCTCTGA
CYP2B6	GGAGTAGAGGCCATACGGGA	AGGAAGGTGGCGTCCATGAG
CYP2D6	CTAAGGGAACGACTCATCAC	CTCACCAGGAAAGCAAAGACAC
CYP2C8	GGACTTTATGGATTGCTTCCTG	CCATATCTCAGAGTGGTGCTTG
CYP2C9	ACTTTCTGGATGAAGGTGGC	GTGCAAAGATGGATAATGCC
CYP2C19	GAACACCAAGAATCGATGGACA	TCAGCAGGAGAAGGAGAGCATA
CYP3A4	CCCTTTGGAAGTGGACCCAG	ACGGTGCCATCCCTTGACTC
HNF1 $\alpha$	TGGGTCCTACGTTACCAAC	TCTGCACAGGTGGCATGAGC
HNF1 $\alpha$ -AS1	AAAGGACCTGGGTCTGCATTC	GTTGACAGGAGCAAACTGCTAAG
AhR	ACATCACCTACGCCAGTCGC	TCTATGCCGCTTGGAAGGAT
CAR	TGATCAGCTGCAAGAGGAGA	AGGCCTAGCAACTTCGCATA
PXR	CAACCTACATGTTCAAAGGCATC	ACACTCCCAGGTTCCAGTCTC
GAPDH	GCACCGTCAAGGCTGAGAAC	TGGTGAAGACGCCAGTGGA



**Supplemental Fig. S1.** The tissue-specific expression patterns of HNF1 $\alpha$  mRNA (A) and HNF1 $\alpha$ -AS1 RNA (B). The data are retrieved from the Gene Expression GTEx database from UCSC. mRNA levels of genes were quantified by RNA-Seq and presented as mean  $\pm$  SD of RPKM (reads per kilobase per million) across 53 human tissues from 714 donors.

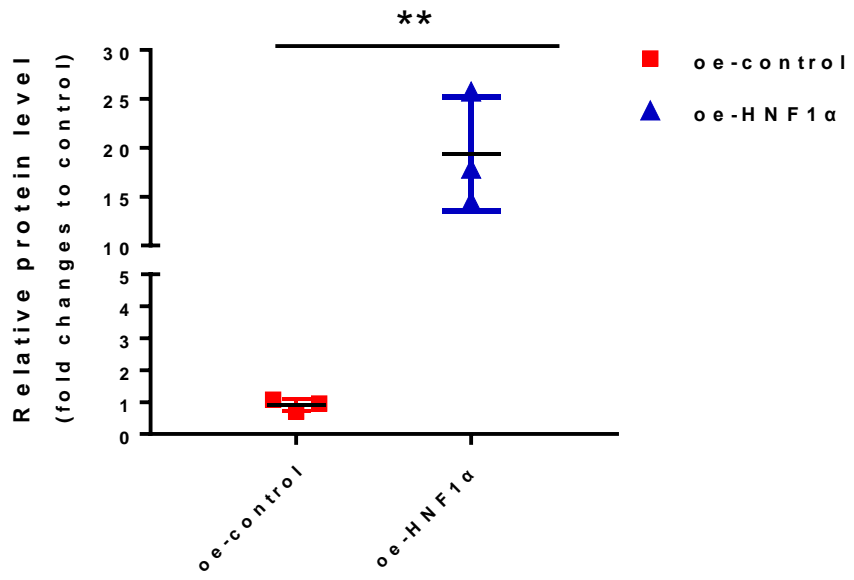


**Supplemental Fig. S2.** The distribution of mRNA expression levels of the tested genes in the 43 human liver tissue samples. (A) The mRNA levels of HNF1 $\alpha$  and HNF1 $\alpha$ -AS1. (B) The mRNA levels of PXR, CAR, and AhR. (C) The mRNA levels of CYP1A2, 2E1, 2B6, and 2C9. (D) The mRNA levels of CYP2D6, 2C8, 2C9, and 3A4. (E) A heat map of the correlation coefficients ( $r$ ) for the mRNA expression levels of different genes, which are calculated by two-tailed Pearson's correlation analysis.

**Supplemental Table S2. Pearson's correlation analysis of the expression between HNF1 $\alpha$ /HNF1 $\alpha$ -AS1 and CYPs as well as transcription regulators**

	HNF1 $\alpha$	HNF1 $\alpha$ -AS1	CYP1A2	2E1	2B6	2D6	2C8	2C9	2C19	3A4	PXR	CAR	AhR
HNF1 $\alpha$	1												
HNF1 $\alpha$ -AS1	0.447**	1											
CYP1A2	0.318*	0.301	1										
CYP2E1	0.216	0.391**	0.243	1									
CYP2B6	0.035	-0.033	0.298	-0.036	1								
CYP2D6	0.294	0.539**	0.342*	0.473**	0.325*	1							
CYP2C8	0.211	0.498**	0.153	0.194	0.281	0.598**	1						
CYP2C9	0.203	0.535**	0.375*	0.087	0.280	0.563**	0.819**	1					
CYP2C19	0.093	0.360*	0.170	0.129	0.182	0.432**	0.784**	0.631**	1				
CYP3A4	0.429**	0.503**	0.385*	0.248	0.368*	0.616**	0.713**	0.651**	0.458**	1			
PXR	0.416**	0.602**	0.334*	0.519**	0.049	0.618**	0.532**	0.504**	0.312*	0.594**	1		
CAR	0.351*	0.676**	0.385*	0.398**	0.274	0.715**	0.663**	0.716**	0.362*	0.654**	0.738**	1	
AhR	0.355*	0.117	0.208	0.174	0.179	0.225	0.299	0.221	0.328*	0.458**	0.299	0.279	1

Pearson's correlation analysis, \* $p$ <0.05, \*\* $p$ <0.01.



**Supplemental Fig. S3.** The protein levels of HNF1 $\alpha$  in control and HNF1 $\alpha$ -overexpression Huh7 cells.

**Supplemental Table S3. Information of liver tissue donors**

Sample number	Age	Sex	Race	Condition
A01	42 y	M	CH	Colorectal metastasis
A02	51 y	M	CH	Hepatocellular carcinoma
A03	46 y	F	CH	Hepatic multiple cyst
A04	67 y	M	CH	Gallbladder carcinoma
A05	48 y	F	CH	Gallbladder carcinoma
A06	63 y	F	CH	Hepatocellular carcinoma
A07	48 y	F	CH	Hepatic hemangioma
A08	59 y	M	CH	Gallbladder carcinoma
A09	54 y	M	CH	Cholangiocarcinoma
A10	58 y	F	CH	Hepatolith
A11	56 y	M	CH	Hepatic hemangioma
A12	50 y	M	CH	Hepatocellular carcinoma
A13	60 y	F	CH	Hepatic hemangioma
A14	46 y	M	CH	Hepatic hemangioma
A15	64 y	F	CH	Gallbladder carcinoma
A16	53 y	M	CH	Hepatolith
A17	56 y	M	CH	Hepatic hemangioma
A18	69 y	F	CH	Gallbladder carcinoma
A19	50 y	F	CH	Hepatolith
A20	45 y	F	CH	Hepatic hemangioma
A21	38 y	F	CH	Hepatic hemangioma

A22	41 y	M	CH	Hepatic hemangioma
A23	61 y	F	CH	Gallbladder carcinoma
A24	37 y	M	CH	Hepatic hemangioma
A25	61 y	F	CH	Hepatic hemangioma
A26	53 y	F	CH	Hepatic hemangioma
A27	45 y	F	CH	Hepatic hemangioma
A28	63 y	M	CH	hepatic metastases
A29	49 y	F	CH	Hepatolith
A30	63 y	M	CH	Hepatocellular carcinoma
A31	43 y	F	CH	Hepatic hemangioma
A32	53 y	F	CH	Hepatic hemangioma
A33	39 y	F	CH	Hepatic hemangioma
A34	47 y	F	CH	Hepatic hemangioma
A35	66 y	M	CH	Esophageal metastasis
A36	41 y	F	CH	Hepatic hemangioma
A37	40 y	F	CH	Hepatic hemangioma
A38	20 y	F	CH	Hepatic hemangioma
A39	59 y	F	CH	Hepatic hemangioma
A40	55 y	F	CH	Hepatic hemangioma
A41	62y	F	CH	Hepatolith
A42	36y	F	CH	Hepatolith
A43	39y	M	CH	Hepatic hemangioma

*A adult , y years , F female , M man*

**Supplemental Table S4.** Characteristics of donors

Number of samples	Race	Stage	Age	Age range	Sex (M:F)
43	CH	Adult	51.1 y	20–69 y	16:27