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Identification of Reactive Metabolites of Acetaminophen and Saxagliptin in Human Hepatocytes and Hepatic Organoids

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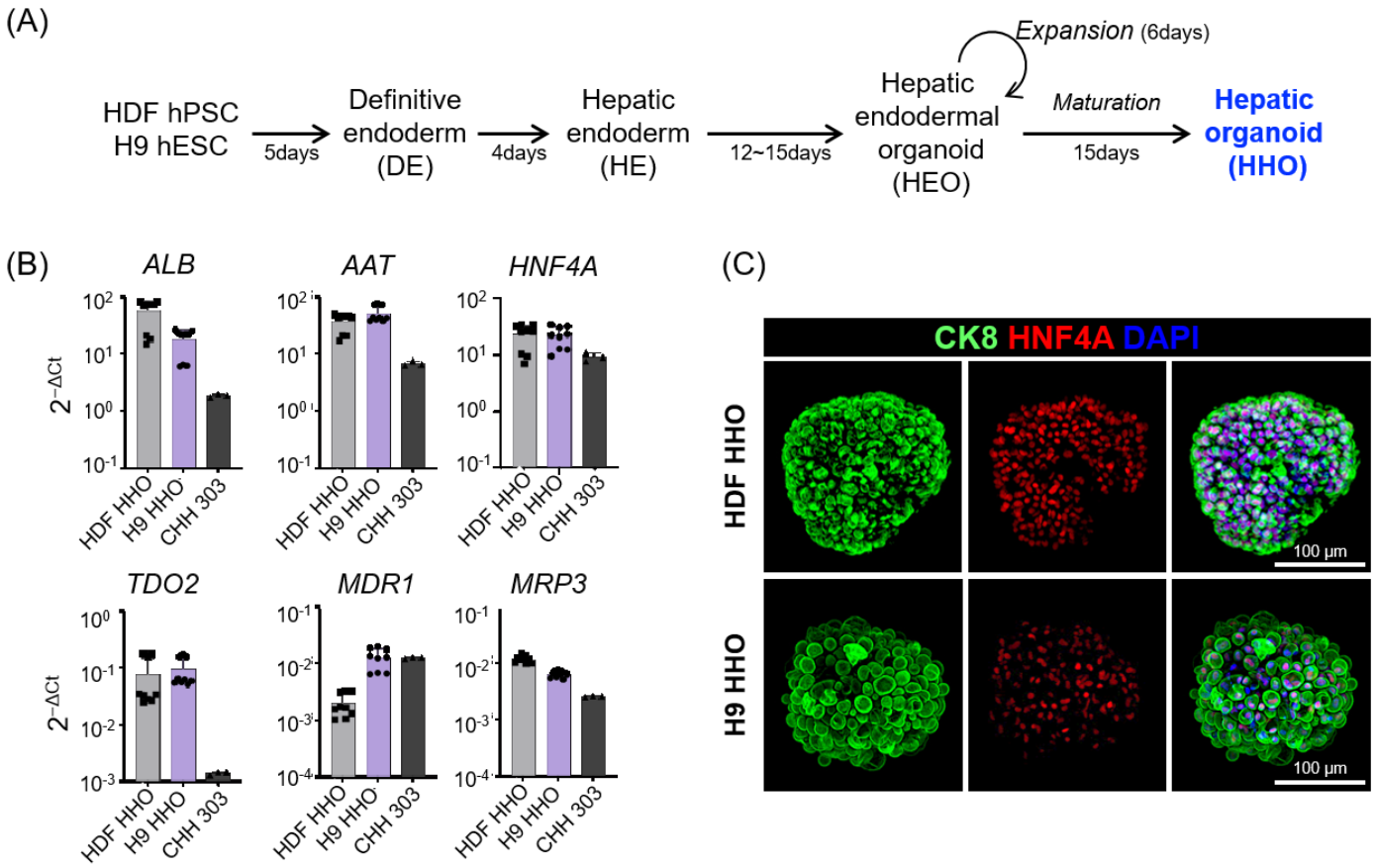
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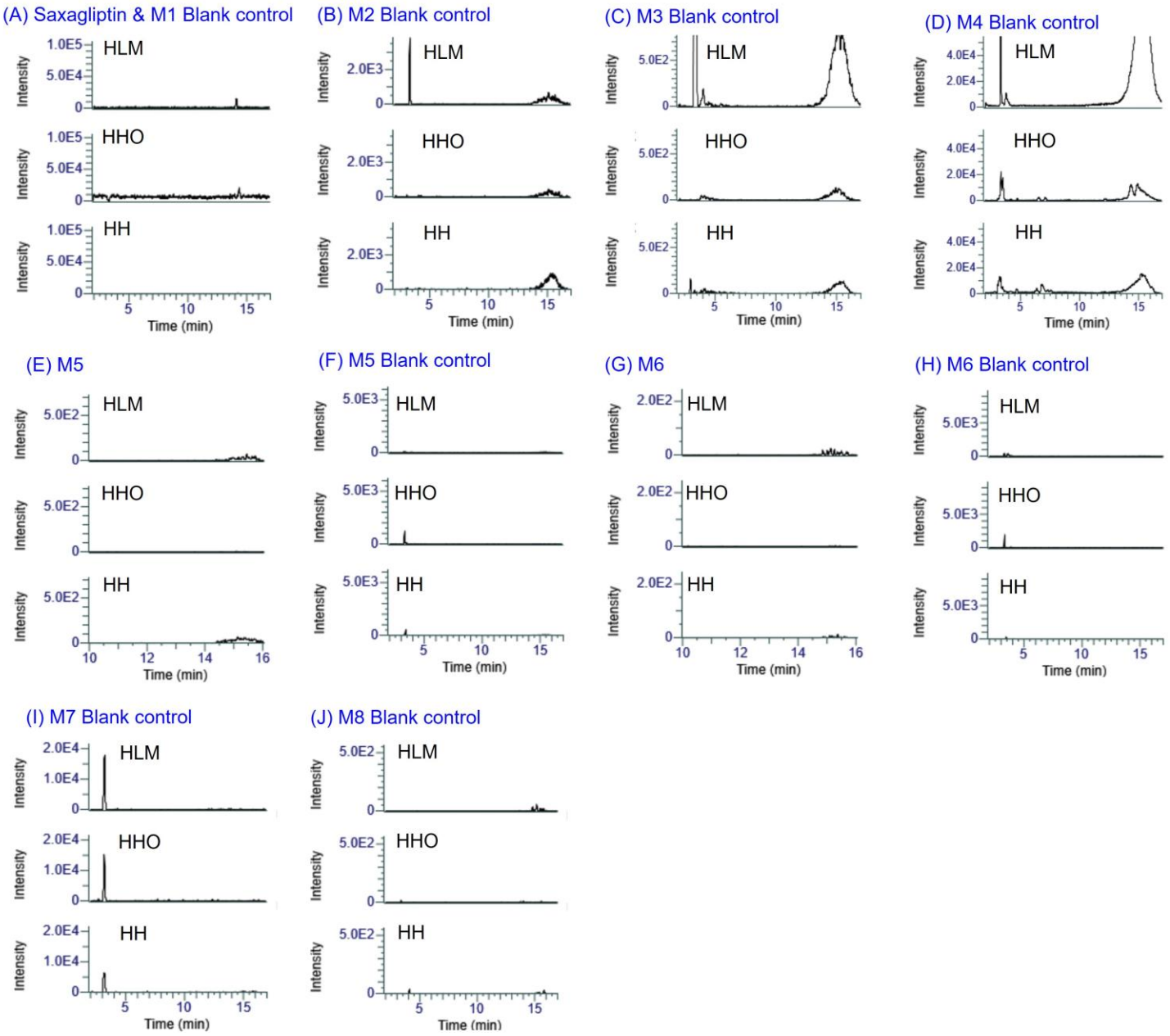
† These authors contributed equally to this work.

Supplementary Table S1. Primers used in RT-qPCR

Gene	NCBI No.	Forward primer	Reverse primer	Product size (bp)
GAPDH	NM_002046	catgagaagtatgacaacagcct	agtccttccacgataccaaagt	113
ALB	NM_000477	gagaccagaggttgatgtgatg	agttccggggcataaaagtaag	114
AAT	NM_000295	gaagtcaaggacaccgagga	gctggcagaccttctgtctt	261
HNF4A	NM_000457	cgaaggtcaagctatgaggaca	atctgcgatgctggcaatct	141
TDO2	NM_005651	caaatcctctgggagttgga	gtccaaggctgtcatcgtct	165
MDR1	NM_000927.4	gggagcttaacacccgactta	gccaaaatcacaagggttagctt	154
MRP3	NM_001144070.1	caccaactcagtcaaacgtgc	gcaagaccatgaaagcgactc	197



Supplementary Figure S1. Differentiation of hepatic organoids from HDF hPSCs and H9 hESCs. (A) Schematic of HHO differentiation. (B) RT-qPCR analysis of hepatic marker gene expression in HDF HHO (P11, P36, and P38), H9 HHO (P5, P12, and P13), and CHH 303. Data are presented as the mean ± SD (n = 3). (C) Representative immunofluorescence images of hepatic markers in HDF HHO-P15 and H9 HHO-P21. Abbreviations: hPSC, human induced pluripotent stem cells; hESC, human embryonic stem cells; HHOs, human hepatic organoids; CHHs, cryopreserved human hepatocytes.



Supplementary Figure S2. Extracted ion chromatograms of saxagliptin and metabolites in HHOs and CHHs after 1 h and 24 h, respectively (A) saxagliptin and M1 blank control, (B) M2 blank control, (C) M3 blank control, (D) M4 blank control, (E) M5, (F) M5 blank control, (G) M6, (H) M6 blank control, (I) M7 blank control, and (J) M8 blank control. Abbreviations: HLMs, human liver microsomes; HHOs, human hepatic organoids; CHHs, cryopreserved human hepatocytes.