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Supporting Information

Copies of HR-ESIMS for 1 and 1s/r; LR-ESIMS for 1A, 1B, 1As/r, 1A's/r, and 1Bs/r; and 1D and 2D NMR spectra for 1, 1s/r, 1A, 1B, 1As/r, 1A's/r, and 1Bs/r; and Figure S1.

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				Mas	ss Spe	ctrum \$	Smartl	For	mula I	Report					
Analysis Info										Acquisition [Date	5/14/201	9 4:36:58	8 PM	
Analysis Name Method Sample Name Comment	D:\Data\MS\data\201905\liwanshan_2 LC_Direct Infusion_pos_70-500mz.m liwanshan_2-37_pos				2-37_pos_35_01_6636.d า				Operator Instrument	SCSIO maXis 255			5552.00029		
Acquisition Param Source Type Focus Scan Begin Scan End	ESI Active 70 m/z 1500 m/z			lon Polarity Set Capillary Set End Plate Offset Set Charging Voltage Set Corona			Positive 4500 V -500 V 0 V 0 nA			Set Nebulizer Set Dry Heater Set Dry Gas Set Divert Valve Set APCI Heater			0.4 Bar 180 °C 4.0 l/min € Waste €r 0 °C		
Intens														+MS, 0.6-0.7	7min #38-39
3-		[M	[+ F 609.3993 	I]+						[M -	+ Na] 31.3823	÷			
1				1					625.3899	629.3656					
600	605		610		615	6	20	1 - 1	625	630		635	·····	640	m/z
Meas. m. 609.395 631.382	/z # Ion F)3 1 C34H)3 1 C34H	ormula 5709 56NaO9	Score 100.00 100.00	m/z 609.3997 631.3817	err [ppm] -0.6 1.0	err [mDa] -0.4 0.6	mSigma 9.0 5.6	rdb 6.5 6.5	e [–] Conf even even	N-Rule ok ok		H 24 ²⁵ 26 23	29 Me 28 27 5 H		
									32 N	OH 12 11 12 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	$ \begin{array}{c} 33 \\ Me \\ 5 \\ 16 \\ 17 \\ 17 \\ 16 \\ 17 \\ 16 \\ 17 \\ 17 \\ 16 \\ 17 \\ 17 \\ 17 \\ 16 \\ 17 \\ 17 \\ 17 \\ 17 \\ 17 \\ 17 \\ 17 \\ 17$	22) 21) 18 19 0 0 0 0 0 0 0 0 0 0 0)	

HR-ESIMS for compound 1

















13 C (175 MHz) NMR spectrum of compound 1 in CD₃OD



13 C (175 MHz) NMR spectrum of compound 1 in CD₃OH



Comparison of ¹³C (175 MHz) NMR spectrum of compound 1 in CD₃OH with that in CD₃OD













¹H–¹H COSY (700 MHz) spectrum of compound **1** in CD₃OD



¹H–¹H COSY (700 MHz) spectrum of compound 1 in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of compound 1 in CD₃OD







ppm

HSQC (700 MHz) spectrum of compound 1 in CD₃OD



HSQC (700 MHz) spectrum of compound 1 in CD₃OD



HSQC (700 MHz) spectrum of compound 1 in CD₃OD





HMBC (700 MHz) spectrum of compound 1 in CD₃OD



HMBC (700 MHz) spectrum of compound 1 in CD₃OD







HMBC (700 MHz) spectrum of compound 1 in CD₃OD





NOESY (700 MHz) spectrum of compound 1 in CD₃OD




S37



NOESY (700 MHz) spectrum of compound 1 in CD₃OD



NOESY (700 MHz) spectrum of compound 1 in CD₃OD



NOESY (700 MHz) spectrum of compound 1 in CD₃OD



2D JRES (700 MHz) spectrum of compound 1 in CD₃OD



2D JRES (700 MHz) spectrum of compound 1 in CD₃OD



2D JRES (700 MHz) spectrum of compound 1 in CD_3OD











UV spectrum of compound 1



S49

LR-ESIMS for the fragment 1A



$[M - H]^-$ 4.4x10^{6_18.592}提取的 277.21 4.2x10⁶ 4.0x10⁶ 3.8x10⁶ OH Me ³² Ме,, 3.6x10⁶ 3.4x10⁶ 6 OH 3.2x10⁶ 3.0x10⁶ 2.8x10⁶ 2.6x10⁶ 2.4x10⁶ Intensity 2.2x10⁶ 2.0x10⁶ 1.8x10⁶ 1.6x10⁶ 1.4x10^{6_} 1.2x10⁶ 1.0x10⁶ 8.0x10⁵ 6.0x10⁵ 4.0x10⁵ 2.0x10⁵ 0.0 200.00 700.00 800.00 900.00 1000.00 1100.00 400.00 500.00 600.00 1200.00 100.00 300 00 m/z

LR-ESIMS for the fragment 1A



¹H (600 MHz) NMR spectrum of the fragment **1A** in CD₃OD



¹H (600 MHz) NMR spectrum of the fragment **1A** in CD₃OD





S55

 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1A** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1A** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1A** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1A** in CD₃OD



LR-ESIMS for the fragment **1B**



LR-ESIMS for the fragment **1B**











 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1B** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1B** in CD₃OD



S67

 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1B** in CD₃OD



S68

 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of the fragment **1B** in CD₃OD



HR-ESIMS for compound 1s

		Mass Spectrum S	SmartFormul	a Report		
Analysis Info			Acquisition Date	Acquisition Date 11/16/2020 4:13:55 PM		
ialysis Name D:\Data\MS\data\202011\jiangzhongping_37-1-R_pos_3_ ethod LC_Direct Infusion_pos_100-3000mz.m ample Name jiangzhongping_37-1-R_pos omment Direct Infusion_pos_100-3000mz.m		_9232.d	Operator SC Instrument ma	CSIO aXis	255552.00029	
Acquisition Param Source Type Socus Scan Begin Scan End	ESI Active 100 m/z 3500 m/z	lon Polarity Set Capillary Set End Plate Offset Set Charging Voltage Set Corona	Positive 4500 V 0 V 0 V 0 V 0 nA	Set Nel Set Dry Set Dry Set Div Set AP	bulizer v Heater v Gas ert Valve CI Heater	0.4 Bar 180 °C 4.0 l/min Waste 0 °C
Intens. x10 ⁵ 1.0-		ГМ н	No1+			+MS, 1.0min
0.8- 0.6- 0.4- 0.2-		1711. 1706.6279	1713.5912	136 1715,5953		
1700.0 Meas. m. 1711.585	' 1705.0' ' 1705.0' /z # Ion Formula S 3 1 C84H91F15NaO19 10	core m/z err [ppm] err [m 10.00 1711.5807 -2.7	1712.5 171 Da] mSigma rdb -4.6 22.5 31.5	1717.5 e ⁻ Conf N-Rule even ok ³² Me ₇ , OR ¹² <u>10</u> ŪR	$H_{1720.0}^{33} H_{1720.0}^{34}$	Me = 0 = 0 $Me = 0$
				R	a = (S)-MTPA	S70

HR-ESIMS for compound 1s



¹H (400 MHz) NMR spectrum of compound **1s** in CDCl₃


¹H (400 MHz) NMR spectrum of compound **1s** in CDCl₃



¹H (400 MHz) NMR spectrum of compound **1s** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1s** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1s** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1s** in CDCl₃



HR-ESIMS for compound 1r

		Mass Spectrum S	SmartFormula	a Report			
Analysis Info				Acquisition Date	e 11/16	11/16/2020 4:17:22 PM	
Analysis Name	D:\Data\MS\data\2020						
Method	hodLC_Direct Infusion_pos_100-3000mz.mple Namejjangzhongping_37-1-S_pos			Operator	SCSIO	CSIO aXis 255552.00029	
Sample Name				Instrument	maXis		
Comment							
Acquisition Param	neter						
Source Type	ESI	Ion Polarity	Positive	S	et Nebulizer	0.4 Bar	
Focus Scan Begin	Active 100 m/z	Set Capillary Set End Plate Offset	4500 V 0 V	S	et Dry Heater et Dry Gas	180 °C 4.0 l/min	
Scan End	3500 m/z	Set Charging Voltage	0 V	S	et Divert Valve	Waste	
		Set Corona	0 nA	S	et APCI Heater	0°C	
Intens x10 ⁵ _						+MS, 1	.1min #60
0.8-		$[\mathbf{N}] + 1$	Naj				
0.6-		1711,58	24				
-							
0.4-		, ,	1713 5800				
-			1715.5656				
0.2-		1706.6256	1714.5914				
			1715.5	5934			
1700.0	1702.5 1705.0	1707.5 1710.0	1712.5 1715.0	1717.5	1720.0	1722.5 1725.0	m/z
Meas m	/z # Ion Formula	Score m/z err [ppm] err [m	Dal mSigma rdb	e ⁻ Conf N-Rule		29	
1711.582	24 1 C84H91F15NaO19	100.00 1711.5807 -1.0	-1.7 26.8 31.5	even ok		Me	
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				OR			
					51		
				D.			
				R	- (<i>r</i> <)-ivi i P <i>P</i>	۱	57

HR-ESIMS for compound 1r



¹H (400 MHz) NMR spectrum of compound **1r** in CDCl₃



¹H (400 MHz) NMR spectrum of compound **1r** in CDCl₃



¹H (400 MHz) NMR spectrum of compound **1r** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1r** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1r** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1r** in CDCl₃



¹H–¹H COSY (400 MHz) spectrum of compound **1r** in CDCl₃



LR-ESIMS for the fragment 1As



¹H (700 MHz) NMR spectrum of the fragment **1As** in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment **1As** in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment **1As** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1As** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1As** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1As** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1As** in CD₃OD



LR-ESIMS for the fragment **1Ar**



¹H (700 MHz) NMR spectrum of the fragment 1Ar in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment 1Ar in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment **1Ar** in CD_3OD







¹H (700 MHz) NMR spectrum of the fragment 1Ar in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1Ar** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1Ar** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1Ar** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1Ar** in CD₃OD



LR-ESIMS for the fragment 1A's



¹H (700 MHz) NMR spectrum of the fragment 1A's in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment 1A's in CD₃OD



¹H (700 MHz) NMR spectrum of the fragment 1A's in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A's** in CD₃OD


$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A's** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A's** in CD₃OD



$^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A's** in CD₃OD



LR-ESIMS for the fragment 1A'r











 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A'r** in CD₃OD



¹H–¹H COSY (700 MHz) spectrum of the fragment **1A'r** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A'r** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (700 MHz) spectrum of the fragment **1A'r** in CD₃OD



LR-ESIMS for fragments 1Bs









 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of fragments **1Bs** in CD₃OD



 $^{1}\text{H}-^{1}\text{H}$ COSY (600 MHz) spectrum of fragments **1Bs** in CD₃OD



¹H–¹H COSY (600 MHz) spectrum of fragments **1Bs** in CD₃OD



¹H–¹H COSY (600 MHz) spectrum of fragments **1Bs** in CD₃OD



LR-ESIMS for fragments 1Br









¹H–¹H COSY (600 MHz) spectrum of fragments **1Br** in CD₃OD



¹H–¹H COSY (600 MHz) spectrum of fragments **1Br** in CD₃OD



¹H–¹H COSY (600 MHz) spectrum of fragments **1Br** in CD₃OD



¹H–¹H COSY (600 MHz) spectrum of fragments **1Br** in CD₃OD





Figure S1. Agonistic effects of chenodeoxycholic acid (the positive control) on hFXR in HepG2 cells