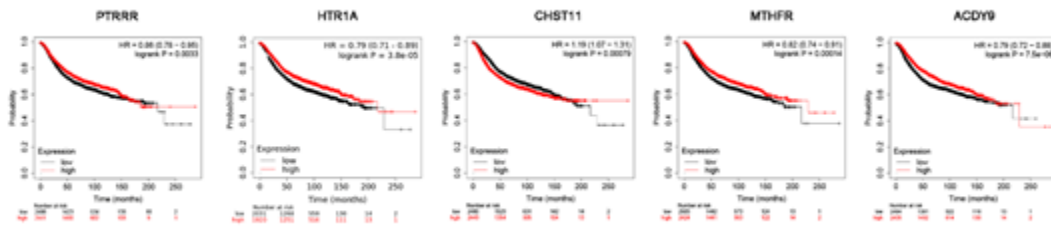


## Supporting Information

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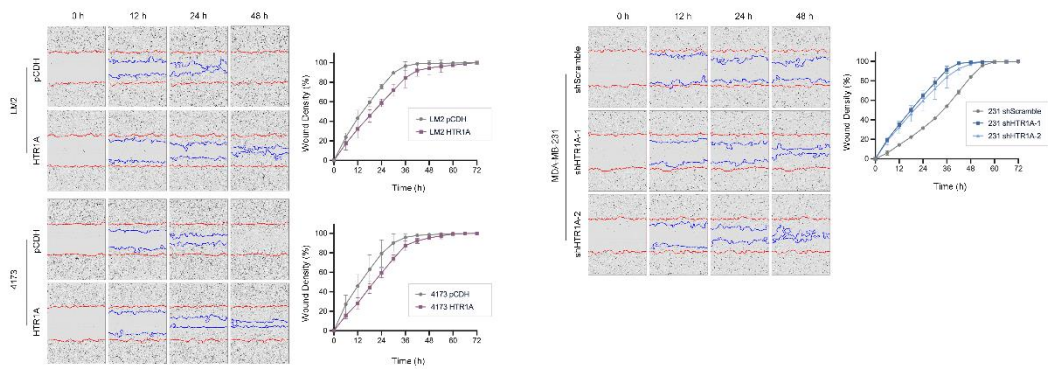
HTR1A Inhibits the Progression of Triple-Negative Breast Cancer via TGF- $\beta$  Canonical and Noncanonical Pathways

*Qiqi Liu, Hefen Sun\**, Yang Liu, Xuan Li, Baojin Xu, Liangdong Li and Wei Jin\*



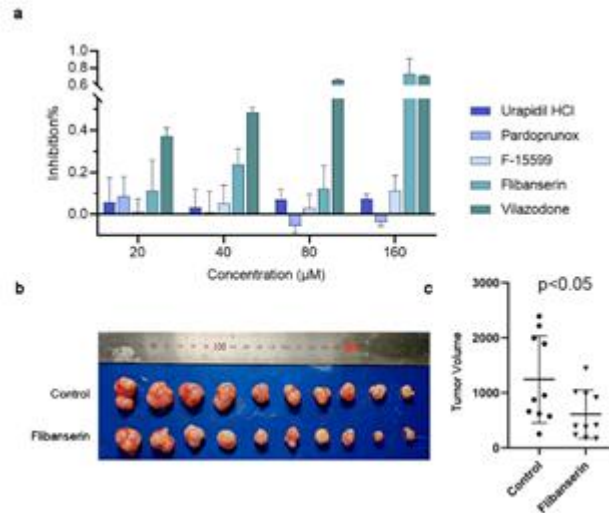
Supplementary Figure 1. The antitumor effect of HTR1A agonists.

The overall survival of indicated genes by the Kaplan-Meier plotter online database.



Supplementary Figure 2. HTR1A inhibited the migration of TNBC cells

The wound healing assay of HTR1A overexpression in LM2 and 4173 cells and HTR1A knockdown in MDA-MB-231 cells.



Supplementary Figure 3. The antitumor effect of HTR1A agonists.

a: The inhibition rate of HTR1A agonists in 48h on LM2 cells by CCK8; b-c: The tumor growth of mouse xenograft models treated with flibanserin and control.

**Supplementary Table 1: The primer sequences of depression-related genes.**

Gene	Primer sequence (5'-3')	Gene	Primer sequence (5'-3')
ACE	GGUGGUAUCUUCGAACCAA	ITPR1	GGACGAGGCUGGAAAUGAA
	TT		TT
	GGUCCAACAUCUAUGACUU		GCACUUUGUUCACUGCAUA
	TT		TT
ADCY9	CCAGGACUCAAGGUGACUU	KLHL29	GCUUUCAAUGUCUGCAAUA
	TT		TT
	GCCAAGAAUCAUAGCCGAU		CCUGAUUGCACACUCCUAU
	TT		TT
APOE	CCAUCAGGAUGGUGUUCUU	LHFPL2	GGAACCCGCAGAACAACAA
	TT		TT
	CCAAGCUGCUGUACGACAU		GCGUCGUGAUAAAGAAAUA
	TT		TT
	GUCACAUUCCUGGCAGGAU		CCGAGCUCAUUGCCUUCAU
	TT		TT

	GAGUUGAAGGCCUACAAAU		GCCAUAGACUACUGUGGAC
	TT		TT
	CGUUGCUGGUCACAUUCCU		GCAGAAAUUGCAACCUCUA
	TT		TT
CHST1	CCACUUGCUUGGGAUCCU	MAOA	GCUGAACCAUGAACAUUUAU
1	TT		TT
	GGUACGGCACCAAGAUCAU		GCAGCUAGGGAGGUCUUA
	TT		TT
	GCAAAGUCUACGAGAACUA		GCUUUACAUCCAGUGCAU
	TT		TT
DNAJB	GGAGAUUUACGACCGCUAU	MTHFR	GCACAUCCGAAGUGAGUUU
2	TT		TT
	GCAGCUGAAGUCAGUCACA		GCCAAUCAAGACAACGAU
	TT		TT
	CCUACAGCCUGUCAGAGAU		CCGGGUUAAUUAACCACCU
	TT		TT
DRD4	GCCUCCAUCUUAACCUGU	PCLO	GCCGAUUCCUAAGCAGCAA
	TT		TT
	GACUACGUGGUCUACUCGU		GCAACAAACUUUGUACCAU
	TT		TT
	CCUUCUUCGUGGUGCACAU		GCAAGAAUCAAGUGUGUAA
	TT		TT
EHD3	CCUUUGGCAACGCCUUCU	PHACTR	GGAGACGCUGACUUCAGAA
	TT	3	TT
	GGAAGGACAACAAGAAGAA		GCGCUGAACGACUCCAUA
	TT		TT
	CCAUGUACGACGAGAUCU		GCAAGCACUUGACAAGAU
	TT		TT
FREM3	GCUUUCAUGGUGGUGUAA	PTPRR	GCUGAACAUAAACCUUGCU
	TT		TT
	GCCCUUCAUCGUUAUAUGAA		CCAACGUAUCUCUUAUUAU
	TT		TT
	GCCAGGUCCUGAUUAUCAA		CCAGUGAGCAGUAUGAAU

	TT		TT
	GGGCAGCAGAAGACUGUAU		UCAACUCCCUGACGAGCUU
GNB3	TT	SLC6A3	TT
	GGUCAUGACCUGUGCCUAU		UCAUCUACCCGGAAGCCAU
	TT		TT
	CCUGGAUGACAACAAUAU		CCAUCUAUGCGGCCUACAA
	TT		TT
	GCAGCCUUGUAGCUGCAA		CCACCGAAAUGGAUGCAUU
HS6ST	TT	SLC6A4	TT
3	GGCUGCUAUAACUUGACUU		GCAUCUGGAAAGGCGUCA
	TT		TT
	GCAUUGAGGAUCUAAACUU		CCUCCUCUUCAUCACGUAU
	TT		TT
	GCGGCAACACUACUGGUAU		CCAAGCCUGAAGUCAGCUU
HTR1A	TT	SLC25A2	TT
	GGCUUAUUGGCUUCCUCAU	1	GCCAUUGCUGGAUUGGGAU
	TT		TT
	GCAACUCCAAAGAGCACUU		GGAGAGAUCAAGUACAGAA
	TT		TT
	GGGUUCCUCAAGCCAACUU		GCAGCUAACACUAAAUA
HTR1B	TT	TPH2	TT
	CCUCGGUCACCUCUAUUA		CCAUGAACUCUUGGGACAU
	TT		TT
	CCAUGUCCAAUGAGGACUU		GCUUACAGGAAUGCCUUAU
	TT		TT
	GCUCUACAGUAAUGACUUU		GCUGUUCUCCCUUCAGUA
HTR2A	TT	UGT2A1	TT
	CCAUGCCAAUACCAGUCUU		GCUUUAGAUGGUAGCCAUU
	TT		TT
	GCUUUGGCCUACAAGUCUA		GCAUAAUGUGACUGUCCUA
	TT		TT
	GCGUGCAGUUUAGAGACAU		GACCUGUUGAACUAUCAGU
HTR3B	TT	VGLL4	TT

	GCUGAUUCCUAGCAUCUUU		CCACGUCUCCAAAAUGAGU
	TT		TT
	GCUUUGACCGACUGCUCUU		GCCUCAGUUACCAAAGAAA
	TT		TT
NC-1	UUCUCCGAACGUGUCACGU	NC-2	GCGACGAUCUGCCUAAGAU
	TT		

**Supplementary Table 2. All antibodies used in this study.**

Antibody	Species	Working concentration	Company
HTR1A	Rabbit	1:1000 for WB, 1:50 for IP	Abcam
TβRII	Mouse	1:2000 for WB, 1:50 for IP	Proteintech
p-Smad3	Rabbit	1:1000 for WB	Abcam
TβR1	Rabbit	1:1000 for WB	Abcam
Smad3	Rabbit	1:1000 for WB	Abcam
Total MEK	Rabbit	1:1000 for WB	CST
Phospho-MEK	Rabbit	1:1000 for WB	CST
Total ERK	Rabbit	1:1000 for WB	Abcam
Phospho-ERK	Rabbit	1:1000 for WB	Abcam
c-Myc	Rabbit	1:1000 for WB	Abcam
E-cadherin	Rabbit	1:1000 for WB	Proteintech
N-cadherin	Rabbit	1:25000 for WB	Proteintech
Fibronectin 1	Mouse	1:1000 for WB	Proteintech
TRIM21	Rabbit	1:1000 for WB, 1:200 for IP	Proteintech
PSMD7	Rabbit	1:1000 for WB, 1:200 for IP	Proteintech

**Supplementary Table 3. The proteins detected by MS/MS.**

Gene Symbol	Full Name	Protein score	Coverage (%)	Peptides	Unique	Avg. Mass
PPP1CC	Serine/threonine-protein phosphatase PP1-gamma catalytic subunit	173.04	37	12	1	36984
RPLP0	60S acidic ribosomal protein P0	163.02	49	11	11	34274
PAWR	PRKC apoptosis WT1 regulator protein	151.84	34	9	9	36568
EEF1A1	Elongation factor 1-alpha 1	148.29	27	9	9	50141

HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	136.46	22	8	8	38434
PSMD7	26S proteasome non-ATPase regulatory subunit 7	123.42	13	5	5	37025
EIF3F	Eukaryotic translation initiation factor 3 subunit F	113.71	14	4	4	37564
HNRNPH3	Heterogeneous nuclear ribonucleoprotein H3	109.8	15	5	5	36926
TRIM21	E3 ubiquitin-protein ligase TRIM21	101.56	17	8	8	54170
JUN	Transcription factor AP-1	90.88	11	3	3	35676
CREB1	Cyclic AMP-responsive element-binding protein 1	83.3	9	3	3	36688
SEC13	Protein SEC13 homolog	79.76	17	4	4	35541
HNRNPA1L2	Heterogeneous nuclear ribonucleoprotein A1-like 2	78.76	9	4	1	34225
CORO1C	Coronin-1C	77.91	8	3	3	53249
EIF3G	Eukaryotic translation initiation factor 3 subunit G	68.07	11	3	3	35611
PLAUR	Urokinase plasminogen activator surface receptor	66.21	10	3	3	36978
WDR77	Methylosome protein 50	63.31	8	2	2	36724
MFGE8	Lactadherin	61.92	9	3	3	43105
CEBPB	CCAAT/enhancer-binding protein beta	58.7	7	1	1	36106
PLAUR	Urokinase plasminogen activator surface receptor	56.51	4	1	1	36978