














Supplementary data to:

Original article:

INHIBITION OF ANGIOTENSIN II TYPE 1 RECEPTOR BY CANDESARTAN REDUCES TUMOR GROWTH AND AMELIORATES FIBROSIS IN COLORECTAL CANCER

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Supplementary Table 1: Candesartan inhibited CRC cell viability (Raw data concerning Figure1A)

Cytotoxic effects of Candesartan on CRC cells						
Candesartan doses (nM)	CT-26 cell viability			SW-480 cell viability		
	0	100.00	98.00	95.00	91.00	96.00
10	73.00	65.00	71.00	75.00	70.00	76.00
50	54.00	49.00	51.00	47.00	44.00	41.00
100	39.00	34.00	31.00	29.00	26.00	34.00
250	22.00	27.00	25.00	25.00	20.00	22.00
500	20.00	14.00	17.00	6.00	10.00	12.00
1000	8.00	10.00	13.00	5.00	8.00	7.00

Supplementary Table 2: 5-FU inhibited CRC cell viability (Raw data concerning Figure1A)

Cytotoxic effects of 5-FU on CRC cells						
5-FU doses (µM)	CT-26 cell viability			SW-480 cell viability		
	0	99.00	93.00	97.00	98.00	91.00
0.1	84.00	81.00	82.00	93.00	84.00	86.00
1	77.00	69.00	73.00	78.00	69.00	74.00
10	65.00	54.00	61.00	57.00	49.00	48.00
50	28.00	37.00	30.00	34.00	42.00	39.00
100	22.00	31.00	28.00	25.00	31.00	32.00
250	20.00	12.00	21.00	16.00	23.00	25.00
500	4.00	8.00	9.00	5.00	14.00	8.00

Supplementary Table 3: Candesartan induced CT-26 cell apoptosis (Raw data concerning Figure1B)

Role of Candesartan on CT-26 cell apoptosis		
Group	Early apoptosis	Late apoptosis
Control	3.38	2.75
Control	0.75	2.12
5-FU	6.07	8.49
5-FU	5.14	7.65
Candesartan	9.53	6.09
Candesartan	8.39	4.21

Supplementary Table 4: Candesartan induced SW-480 cell apoptosis (Raw data concerning Figure1B)

Role of Candesartan on SW-480 cell apoptosis		
Group	Early apoptosis	Late apoptosis
Control	2.55	1.47
Control	2.28	0.71
5-FU	8.46	27.39
5-FU	9.23	31.3
Candesartan	0.11	0.21
Candesartan	3.68	1.44

Supplementary Table 5: The effect of Candesartan in E-cadherin expression in mRNA levels (Raw data concerning Figure 2B)

Group	E-cadherin mRNA levels		
	1	1	1
Control	1	1	1
5-FU	1.8	1.67	1.84
Candesartan	1.37	1.55	1.49

Supplementary Table 6: The effect of Candesartan in MMP3 expression in mRNA levels (Raw data concerning Figure 2B)

Group	MMP3 mRNA levels		
	1	1	1
Control	1	1	1
5-FU	0.33	0.56	0.49
Candesartan	1.1	0.8	0.92

Supplementary Table 7: The effect of Candesartan in MMP9 expression in mRNA levels (Raw data concerning Figure 2B)

Group	MMP9 mRNA levels		
	1	1	1
Control	1	1	1
5-FU	0.36	0.2	0.39
Candesartan	0.56	0.71	0.58

Supplementary Table 8: Candesartan reduced tumor growth in xenograft model (Raw data concerning Figure 3B)

Group	Tumor size (mm ³)							
	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14
Control	140.13	309.57	530.01	851.73	1474.79	1831.54	3240.00	3528.00
Control	123.76	193.21	223.51	449.64	856.24	1275.57	1493.00	1752.00
Control	126.10	181.50	457.40	524.37	845.37	1832.08	3283.56	3414.32
Control	135.11	195.35	455.30	560.79	1862.91	1754.44	2501.00	3190.84
Control	327.20	645.39	1274.78	1798.72	1900.28	2001.20	2156.32	2366.44
Control	380.72	772.09	1139.95	1588.84	1921.10	2412.01	2912.00	3396.72
5-FU	115.34	141.45	292.39	548.87	804.94	1611.06	1000.00	1590.94
5-FU	118.52	210.90	274.86	303.49	585.00	862.49	873.98	1172.41
5-FU	115.54	151.23	236.69	443.45	1106.21	1730.56	2148.10	2355.43
5-FU	107.43	161.88	251.23	437.77	975.78	1588.15	2802.30	3256.19
5-FU	135.21	119.19	149.46	262.92	568.92	1361.70	1731.68	1897.21
5-FU	167.26	401.33	572.27	1228.09	1889.29	2123.00	2684.41	2721.25
Candesartan	70.19	93.41	84.15	188.69	711.00	1020.00	1290.00	1305.95
Candesartan	95.72	120.46	144.83	176.33	765.00	1120.00	1360.00	1401.00
Candesartan	88.06	81.45	183.18	252.45	505.66	709.91	1353.42	1525.13
Candesartan	99.50	129.35	226.74	304.13	451.34	754.74	1310.44	1310.00
Candesartan	98.00	127.00	201.00	298.00	501.00	810.00	1305.00	1401.00
Candesartan	87.00	131.00	199.00	302.00	498.00	801.00	1320.00	1430.00
Candesartan+5-FU	96.24	117.95	121.29	281.69	239.39	742.94	1024.67	1228.81
Candesartan+5-FU	97.15	111.73	205.97	307.37	808.70	1357.67	1500.00	1646.00
Candesartan+5-FU	102.06	157.42	227.72	276.30	359.51	309.83	701.84	987.74
Candesartan+5-FU	81.30	114.56	115.00	265.00	376.00	687.00	1201.00	1198.00
Candesartan+5-FU	87.00	132.00	154.00	281.69	399.00	742.94	1021.00	1321.00
Candesartan+5-FU	99.00	139.00	231.00	276.30	299.00	310.00	720.00	1001.00

Supplementary Table 9: Candesartan reduced tumor weight in xenograft model (Raw data concerning Figure 3C)

Group	Tumor weight (g)
Control	3.82
Control	1.97
Control	4.07
Control	3.48
Control	2.90
Control	3.60
5-FU	1.80
5-FU	1.28
5-FU	2.17
5-FU	4.23
5-FU	1.95
5-FU	3.41
Candesartan	1.89
Candesartan	1.89
Candesartan	1.91
Candesartan	1.89
Candesartan	1.88
Candesartan	1.96
Candesartan+5-FU	1.93
Candesartan+5-FU	1.23
Candesartan+5-FU	1.09
Candesartan+5-FU	1.42
Candesartan+5-FU	1.62
Candesartan+5-FU	1.23

Supplementary Table 10: The effect of Candesartan in Cyclin D1 expression in mRNA levels (Raw data concerning Figure 3E)

Group	Cyclin D1 mRNA levels		
Control	1	1	1
5-FU	0.15	0.27	0.33
Candesartan	0.65	0.48	0.61

Supplementary Table 11: The effect of Candesartan in Survivin expression in mRNA levels (Raw data concerning Figure 3E)

Group	Survivin mRNA levels		
Control	1	1	1
5-FU	0.25	0.45	0.3
Candesartan	0.86	0.81	0.79

Supplementary Table 12: The effect of Candesartan in Collagen content in tumor tissues (Raw data concerning Figure 4B)

Group	Collagen content
Control	25.00
Control	20.00
Control	18.00
Control	28.00
Control	31.00
Control	25.00
5-FU	15.00
5-FU	13.00
5-FU	14.00
5-FU	10.00
5-FU	11.00
5-FU	14.00
Candesartan	7.00
Candesartan	5.00
Candesartan	6.00
Candesartan	6.00
Candesartan	4.00
Candesartan	5.00
Candesartan+5-FU	3.00
Candesartan+5-FU	2.00
Candesartan+5-FU	4.00
Candesartan+5-FU	3.00
Candesartan+5-FU	2.00
Candesartan+5-FU	5.00

Supplementary Table 13: The effect of Candesartan on the enzymatic activity of SOD, catalase, MDA, and total thiol in tumor tissues (Raw data concerning Figure 5A-D)

Group	SOD activity (U/g tissue)	CAT activity (U/g tissue)	MDA (nmol/g tissue)	Thiol (μmol/g tissue)
Control	5.96	.80	5.08	.98
Control	4.26	.55	6.73	1.69
Control	4.53	.50	6.41	1.01
Control	4.87	.59	6.67	.91
Control	4.45	.57	5.51	.97
Control	5.62	.67	5.13	1.58
5-FU	4.00	.35	8.85	.89
5-FU	4.18	.41	7.05	.54
5-FU	4.53	.40	7.56	.49
5-FU	3.50	.41	8.33	.76
5-FU	3.96	.39	8.27	.71
5-FU	4.03	.42	7.56	.54
Candesartan	3.62	.31	8.65	.44
Candesartan	3.17	.35	7.95	.47
Candesartan	3.31	.33	7.82	.42
Candesartan	3.10	.32	8.10	.40
Candesartan	3.30	.36	8.30	.44
Candesartan	3.20	.29	8.20	.43
Candesartan+5-FU	2.34	.25	9.04	.11
Candesartan+5-FU	2.18	.31	8.14	.19
Candesartan+5-FU	2.08	.29	8.65	.24
Candesartan+5-FU	1.90	.28	8.40	.20
Candesartan+5-FU	2.10	.27	8.30	.13
Candesartan+5-FU	2.00	.27	8.33	.14

Supplementary Table 14: The effect of Candesartan in inflammatory cytokines in tumor tissues (Raw data concerning Figure 5E)

Group	TNF- α (pg/ml)		
	1	1	1
Control	1	1	1
5-FU	0.4	0.21	0.29
Candesartan	0.55	0.48	0.52

Supplementary Table 15: The effect of Candesartan in inflammatory cytokines in tumor tissues (Raw data concerning Figure 5E)

Group	IL-6 (pg/ml)		
	1	1	1
Control	1	1	1
5-FU	0.39	0.57	0.51
Candesartan	0.76	0.98	0.9