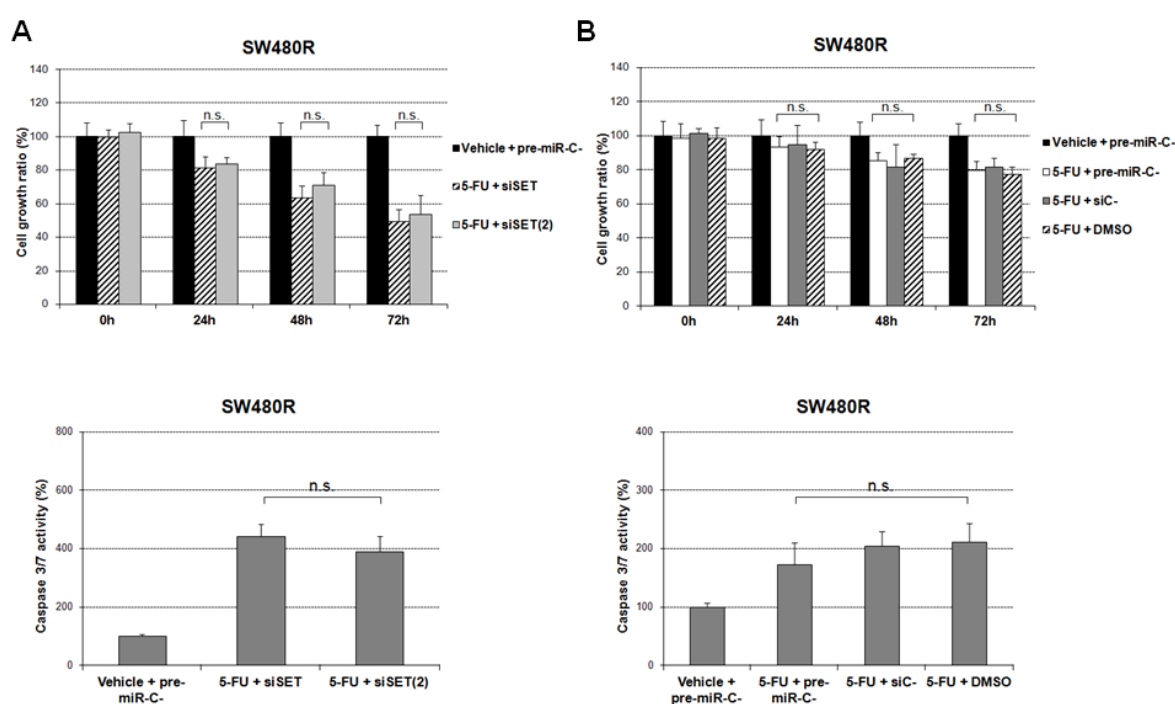


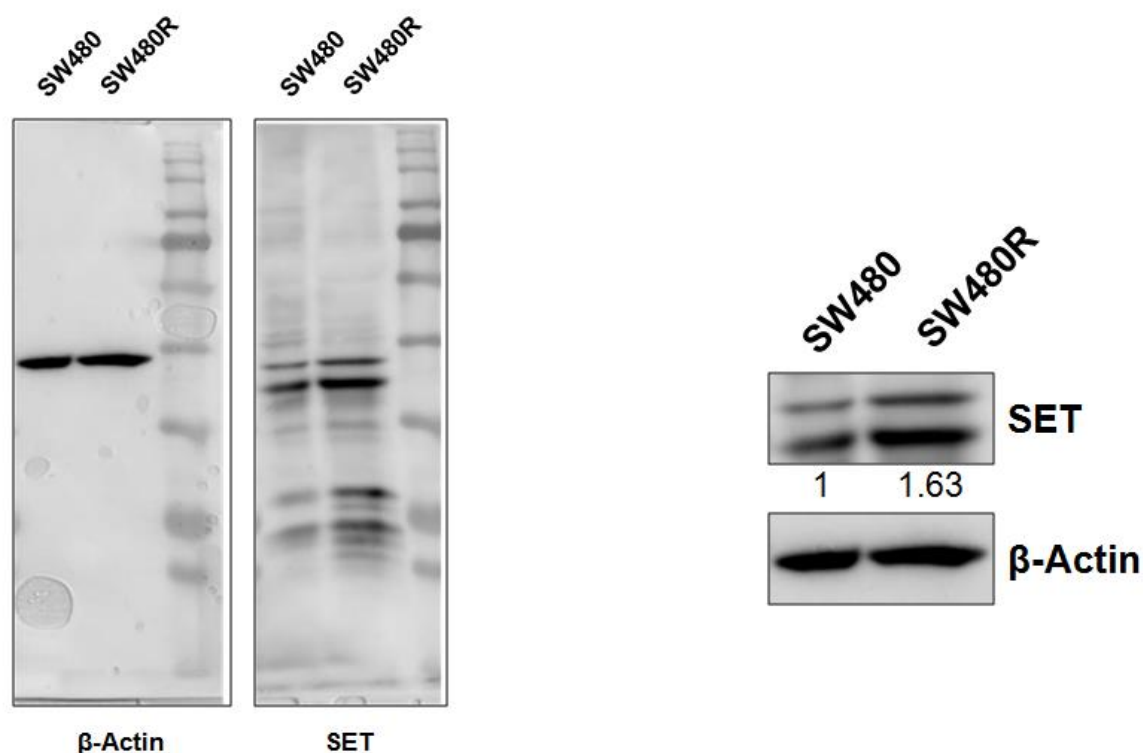
Supplementary Materials

## MicroRNA-199b downregulation confers resistance to 5-fluorouracil treatment and predicts poor outcome and response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer patients

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**Figure S1.** Controls for MTS and caspase 3/7 assays using (A) two specific SET siRNAs and (B) negative controls for miR-199b, siSET and FTY720.



**Figure S2.** Detailed information about SET analysis by western blot.

**Table S1.** Association between miR-199b and clinical and molecular parameters in 110 LARC patients.

Parameters	No. Cases	No. miR-199b High (%)	No. miR-199 Low (%)	<i>p</i>
MiR-199b	110	81 (73.6)	29 (26.4)	
Age	110	81	29	0.919
< 70	56	41 (73.2)	15 (26.8)	
≥ 70	54	40 (74.1)	14 (25.9)	
ECOG	110	81	29	0.300
0	67	47 (70.1)	20 (29.9)	
1-2	43	34 (79.1)	9 (20.9)	
Stage	110	81	29	0.547
I-II	15	12 (80)	3 (20)	
III	95	69 (72.6)	26 (27.4)	

**Table S2.** Association between miR-199b and tumor size/lymph node positivity in 82 LARC patients.

Parameters	No. Cases	No. miR-199b High (%)	No. miR-199 Low (%)	<i>p</i>
ypT	82	58	24	0.015
0-1	22	20 (34.5)	2 (8.3)	
> 1	60	38 (65.5)	22 (91.7)	
ypN	82	58	24	0.006
N0	64	50 (86.2)	14 (58.3)	
N+	18	8 (13.8)	10 (41.7)	

**Table S3.** Association between miR-199b expression levels and downgrading in 60 LARC patients.

MiR-199b Expression	No. Cases	MiR-199b Low (%)	MiR-199b High (%)	<i>p</i>
Downgrading	60	21	39	0.004
No	40	19 (90.5)	21 (53.8)	
Yes	20	2 (9.5)	18 (46.2)	

**Table S4.** Association between miR-199b and SET expression levels in LARC patients.

Parameters	No. Cases	MiR-199b Low (%)	MiR-199b High (%)	<i>p</i>
SET	76	23	53	0.004
Low	59	13 (56.5)	46 (86.8)	
High	17	10 (43.5)	7 (13.2)	

**Table S5.** Association between SET expression levels and pathological response to neoadjuvant CRT in LARC patients.

Responders vs. Non-Responders				
SET Expression	No. Cases	SET Low (%)	SET High (%)	<i>p</i>
Response	76	59	17	0.015
Non-Response <sup>1</sup>	34	22 (37.3)	12 (70.6)	
Response <sup>2</sup>	42	37 (62.7)	5 (29.4)	

<sup>1</sup>Non-Response: poor or minimal pathological response; <sup>2</sup>Response: moderate or complete pathological response.

**Table S6.** Association between miR-199b and immunohistochemical SET expression in LARC patients.

Parameters	No. Cases	MiR-199b Low (%)	MiR-199b High (%)	<i>p</i>
SET	20	4	16	0.028
Low	17	2 (50)	15 (93.7)	
High	3	2 (50)	1 (6.3)	

**Table S7.** Univariate and multivariate Cox analyses in the cohort of 82 LARC patients.

Parameters	Univariate EFS <sup>1</sup> Analysis			Multivariate EFS Cox Analysis		
	HR <sup>3</sup>	95% CI <sup>2</sup>		HR	95% CI	
		Lower	Upper		Lower	Upper
Age						
< 70	1.000			1.000		
≥ 70	1.573	0.514 to 4.817		1.686	0.520 to 5.468	
Gender						
Male	1.000					
Female	0.976	0.318 to 2.997		-	-	
Pathological Stage						
0-I	1.000					
II-III	2.050	0.666 to 6.313		-	-	
ypT <sup>4</sup>						
0-2	1.000					
3-4	1.318	0.906 to 1.916		-	-	
ypN <sup>5</sup>						
N-	1.000			1.000		
N+	3.522	1.057 to 11.738		2.045	0.929 to 4.504	
ECOG <sup>6</sup>						
0	1.000					
1-2	1.702	0.570 to 5.081		-	-	
MiR-199b						
High	1.000			1.000		
Low	3.744	1.226 to 11.428		3.360	1.042 to 10.831	

<sup>1</sup>EFS: event-free survival; <sup>2</sup>CI: confidence interval; <sup>3</sup>HR: Hazard ratio; <sup>4</sup>ypT: tumor size after chemoradiotherapy (CRT); <sup>5</sup>ypN: pathological lymph node after CRT; <sup>6</sup>ECOG: Eastern Cooperative Oncology Group.



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