

MicroRNA-19b plays a key role in 5-fluorouracil resistance and predicts tumor progression in locally advanced rectal cancer patients

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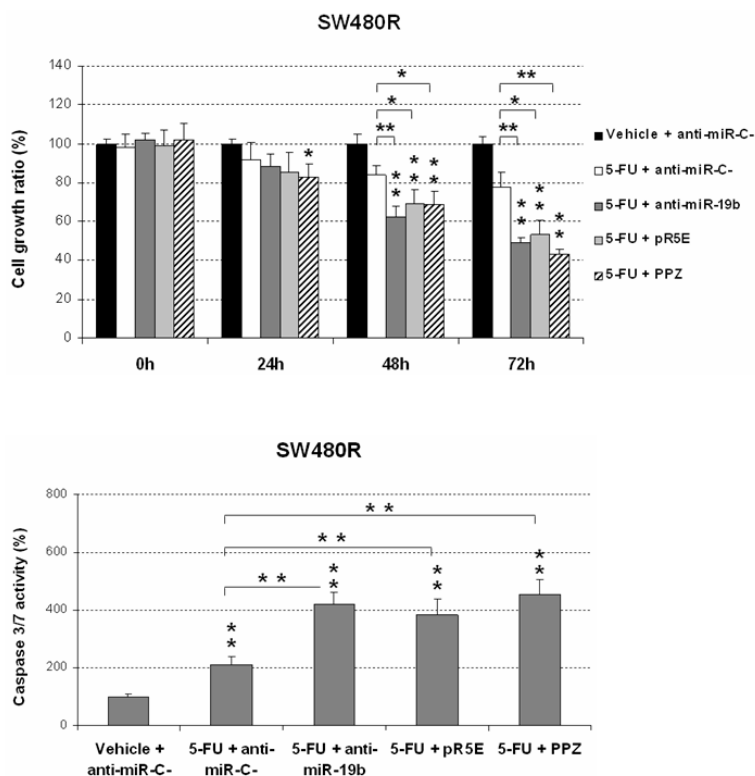


Figure S1. MTS and caspase-activation assays showing that the miR-19b/PPP2R5E signaling axis emerges as a novel therapeutic target to overcome 5-FU resistance; *P < 0.05; **P < 0.01. Asterisks over the columns refer comparison of each condition against control (first column).

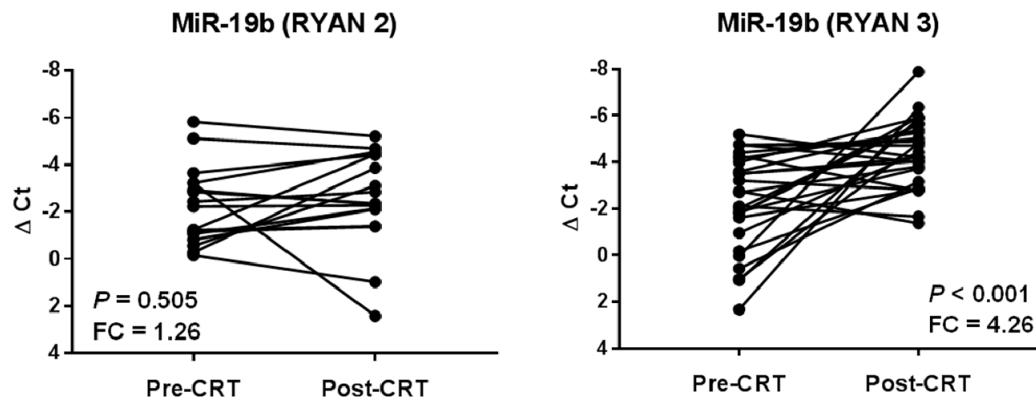


Figure S2. Scatter plots showing miR-19b expression in pre- and post-preoperative CRT samples from each LARC patient of our global cohort. FC = fold change.

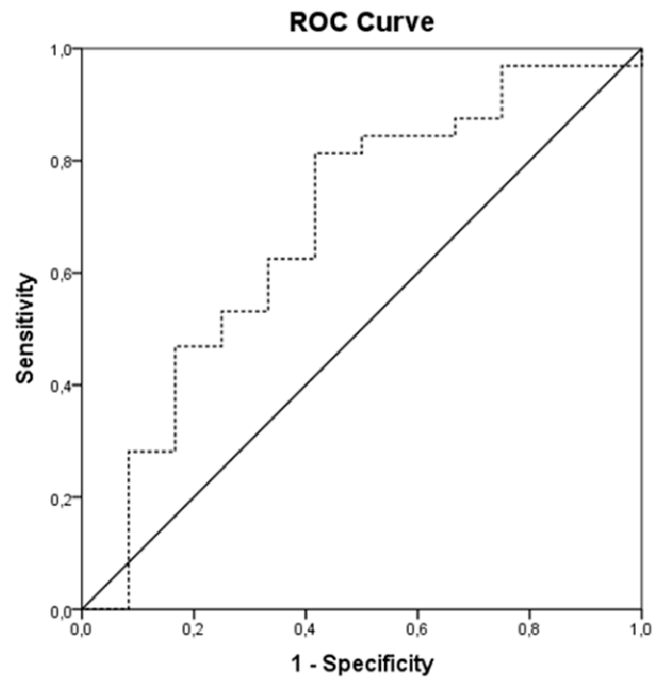


Figure S3. Receiver operating characteristic (ROC) curve to assess the usefulness of miR-19b to discriminate patient recurrence in post-treatment samples from LARC patients that have a lack of response to neoadjuvant CRT. The dashed line represents the coordinated points of the ROC curve. The solid line is the diagonal reference line.

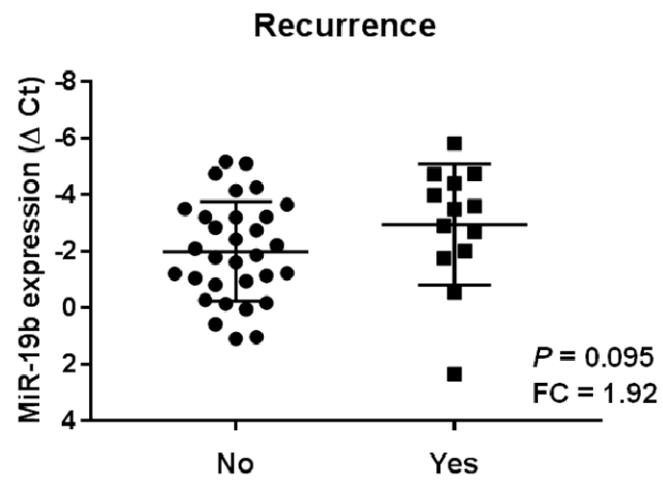


Figure S4. MiR-19b expression levels in pre-CRT samples from LARC patients with and without disease relapse in our global cohort. FC = fold change.

Table S1. Clinical characteristics of a series of 44 LARC patients with paired pre- and post-neoadjuvant CRT biopsies available.

		No. (%)
Sex		
	Male	28 (63.6)
	Female	16 (36.4)
Age		
	<70	27 (61.4)
	≥70	17 (38.6)
ECOG ¹		
	0	29 (65.9)
	≥1	15 (34.1)
Site of primary tumor		
	Rectum	44 (100)
Clinical stage pre-CRT ²		
	II	3 (6.8)
	III	41 (93.2)
Grade pre-CRT		
	Low	18 (40.9)
	Moderate-High	26 (59.1)
Pathological response		
	RYAN 2	17 (38.6)
	RYAN 3	27 (61.4)

¹ECOG = Eastern Cooperative Oncology Group; ²CRT = Chemoradiotherapy; RYAN 2 = residual cancer outgrown by fibrosis; RYAN 3 = minimal or no tumor kill and extensive residual cancer.

Table S2. Association between local and distant recurrence and miR-19b expression in post-treatment biopsies from non-responder LARC patients to neoadjuvant CRT.

Parameter	No. Cases	No (%)	Yes (%)	<i>p</i>
MiR-19b overexpression	44	30	14	
Local recurrence	44	30	14	0.004
No	38	29 (76.3)	9 (23.7)	
Yes	6	1 (16.7)	5 (83.3)	
Distant metastasis	44	30	14	0.009
No	33	26 (78.8)	7 (21.2)	
Yes	11	4 (36.4)	7 (63.6)	