Supplementary Materials: Tumor Long Interspersed Nucleotide Element-1 (LINE-1) Hypomethylation in Relation to Age of Colorectal Cancer Diagnosis and Prognosis

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Table S1. Linear regression analysis to predict LINE-1 methylation level (outcome) by four age groups (predictor) using indicator variables for missing data.

Variables in the model	β coefficient [a] (change in mean LINE-1 methylation levels by a given variable)			
	Univariable (unadjusted) (95% CI)	*P* value	Multivariable-adjusted [b] (95% CI)	*P* value
Age at diagnosis		< 0.0001 [c]		0.0002 [c]
<50	−5.87 (−9.65 to −2.09)		−4.79 (−8.49 to −1.10)	
50–54	−3.70 (−6.23 to −1.17)		−2.84 (−5.32 to −0.37)	
55–69	−1.90 (−3.00 to −0.80)		−1.38 (−2.47 to −0.30)	
≥70	Referent		Referent	
Family history of colorectal cancer		0.13		0.028
Absent	Referent		Referent	
Present	−1.03 (−2.37 to 0.31)		−1.45 (−2.75 to −0.15)	
MSI status		< 0.0001		0.0007
Non-MSI-high	Referent		Referent	
MSI-high	5.73 (4.30 to 7.16)		3.20 (1.35 to 5.06)	
CIMP status		<0.0001		<0.0001
Negative/low	Referent		Referent	
High	6.00 (4.61 to 7.39)		3.72 (1.90 to 5.55)	

[a] The β coefficient represents a change (increase or decrease) in mean LINE-1 methylation level by a given variable. [b] The multivariable linear regression model initially included age, family history of colorectal cancer in any first-degree relative, MSI status, and CIMP status. [c] P_{trend} was calculated by the linear trend across the ordinal age variable (≥70, 55–69, 50–54, and <50) in the linear regression model.–Abbreviations: CI, confidential interval; CIMP, CpG island methylator phenotype; LINE-1, long interspersed nucleotide element-1; MSI, microsatellite instability.

Table S2. LINE-1 methylation level of colorectal cancer cases according to age at diagnosis.

LINE-1 methylation level [0 to 100 (percent) scale]	Total No. (*n* = 1356)	Age at diagnosis						*P* value *
		<50 (*n* = 28)	50–54 (*n* = 66)	55–59 (*n* = 122)	60–64 (*n* = 191)	65–69 (*n* = 301)	≥70 (*n* = 648)	
								<0.0001
mean ± SD	63.6 ± 10.1	58.9 ± 12.0	61.0 ± 10.2	61.3 ± 10.3	61.7 ± 8.90	64.2 ± 9.07	64.7 ± 10.4	
								<0.0001
≤45	47 (3.5%)	5 (18%)	2 (3.0%)	8 (6.6%)	5 (2.6%)	8 (2.7%)	19 (2.9%)	
45–55	206 (15%)	4 (14%)	15 (23%)	23 (19%)	40 (21%)	35 (12%)	89 (14%)	
55–65	499 (37%)	10 (36%)	23 (35%)	41 (34%)	83 (43%)	121 (40%)	221 (34%)	
>65	604 (45%)	9 (32%)	26 (39%)	50 (41%)	63 (33%)	137 (45%)	319 (49%)	

* Spearman's correlation test was used to examine the association between six age groups (≥70, 65–69, 60–64, 55–60, 50–54, and <50) and categorical data (or continuous value) of LINE-1 methylation level. Abbreviations: LINE-1, long interspersed nucleotide element-1; SD, standard deviation.