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ABSTRACT

Most patients with oral squamous cell cancer (OSCC) have a locally advanced stage at diagnosis. The treatment strategies are diverse, including surgery, radiotherapy and chemotherapy. Despite multimodality treatment, the response rate is unsatisfactory. DNA repair and genetic instability are highly associated with carcinogenesis and treatment outcomes in oral squamous cell cancer, affecting cell growth and proliferation. Therefore, focusing on DNA repair and genetic instability interactions could be a potential target for improving the outcomes of OSCC patients.

DNA polymerase β (POLB) is an important enzyme in base excision repair and contributes to gene instability, leading to tumorigenesis and cancer metastasis. The aim of our study was to confirm POLB regulates the growth of OSCC cells through modulation of cell cycle and chromosomal instability.

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RESULTS

We analyzed a tissue array from 133 OSCC patients and discovered that low POLB expression was associated with advanced tumor stage and poor overall survival. In multivariate Cox proportional hazards regression analysis, low POLB expression and advanced lymph node status were significantly associated with poor survival. By performing in vitro studies on model cell lines, we demonstrated that POLB silencing regulated cell cycles, exacerbated mitotic abnormalities and enhanced cell proliferation. After POLB depletion, OSCC cells showed chromosomal instability and aneuploidy.

In conclusion, POLB is an important maintainer of karyotypic stability in OSCC cells.

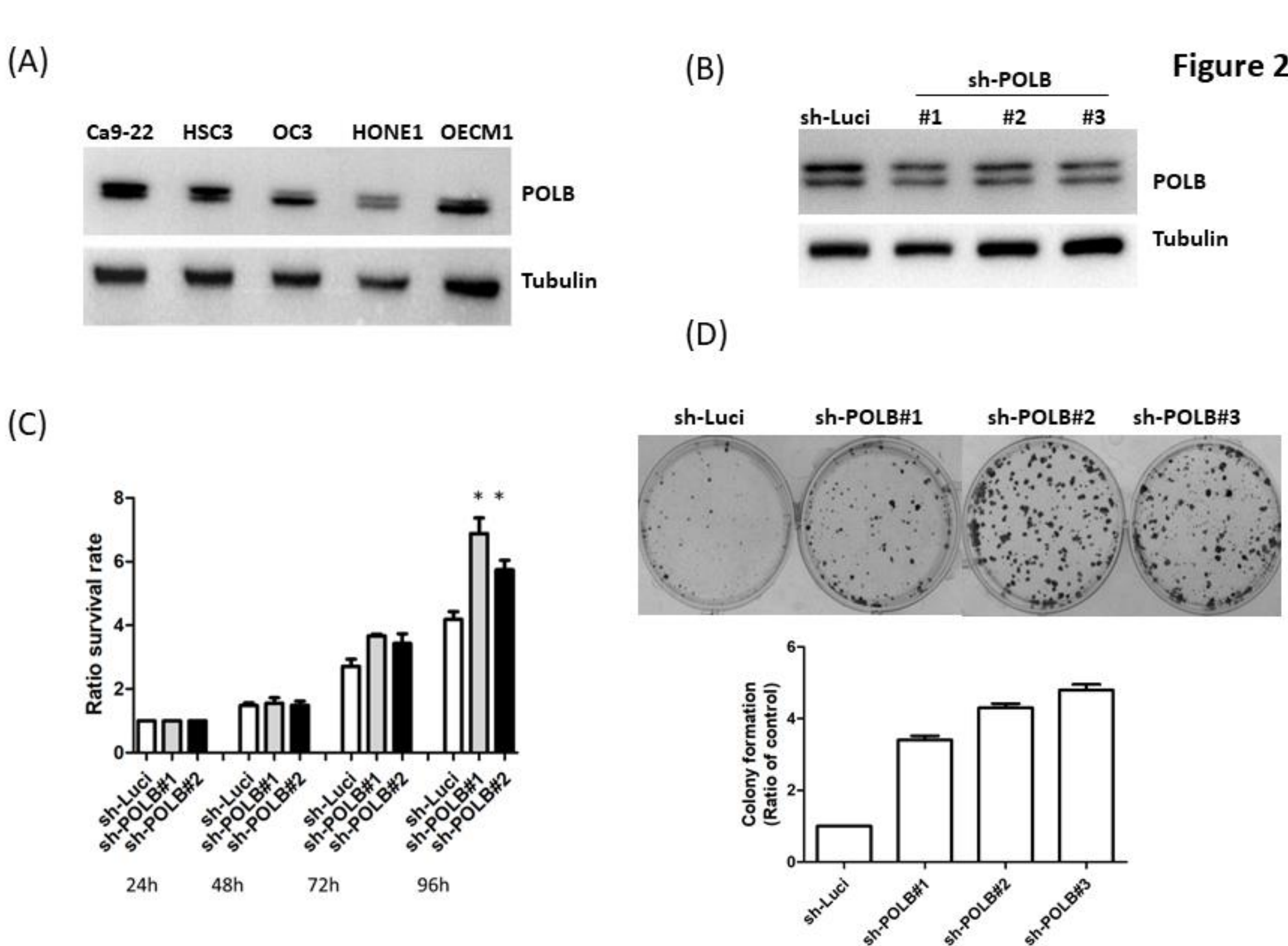
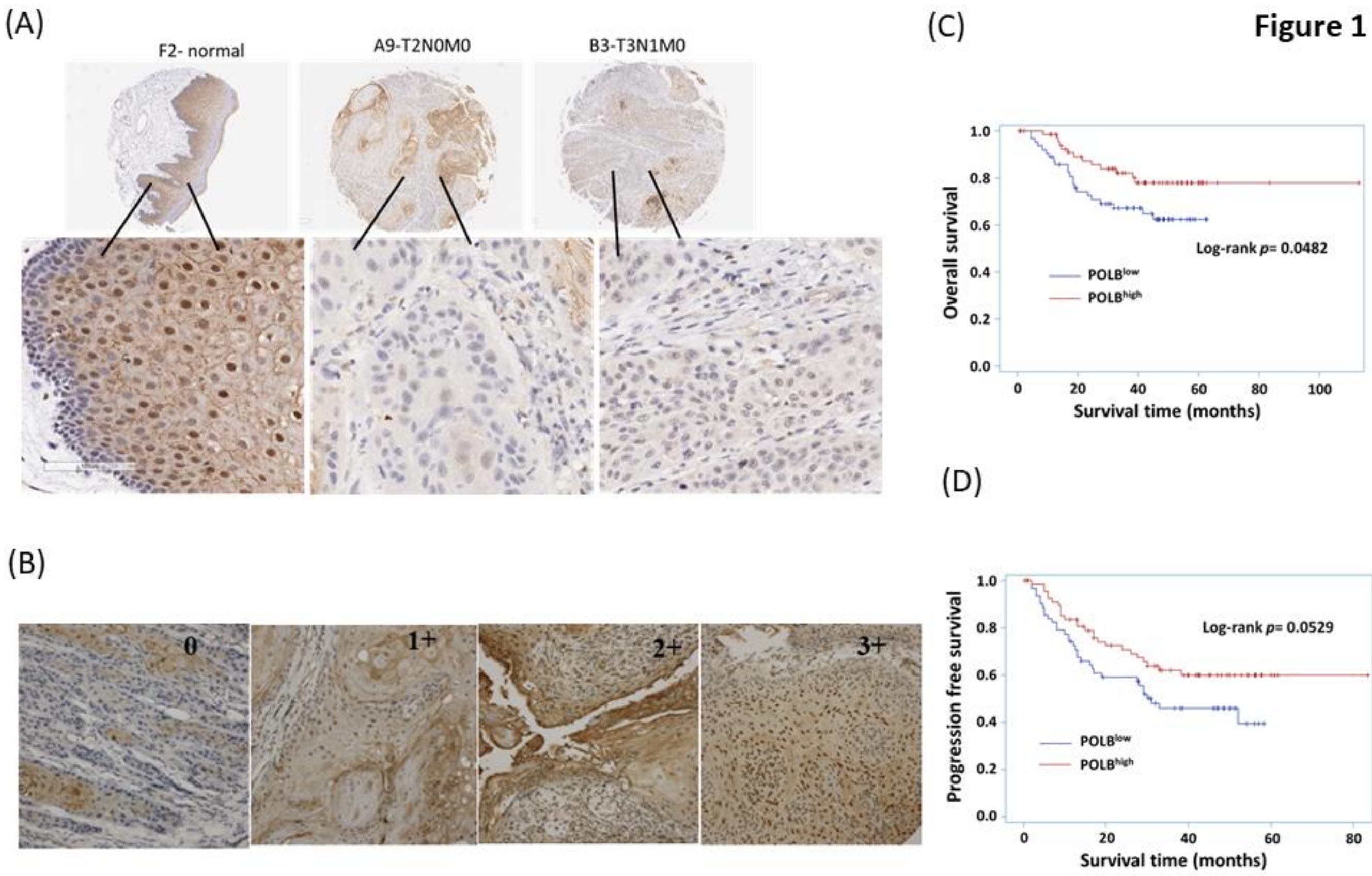


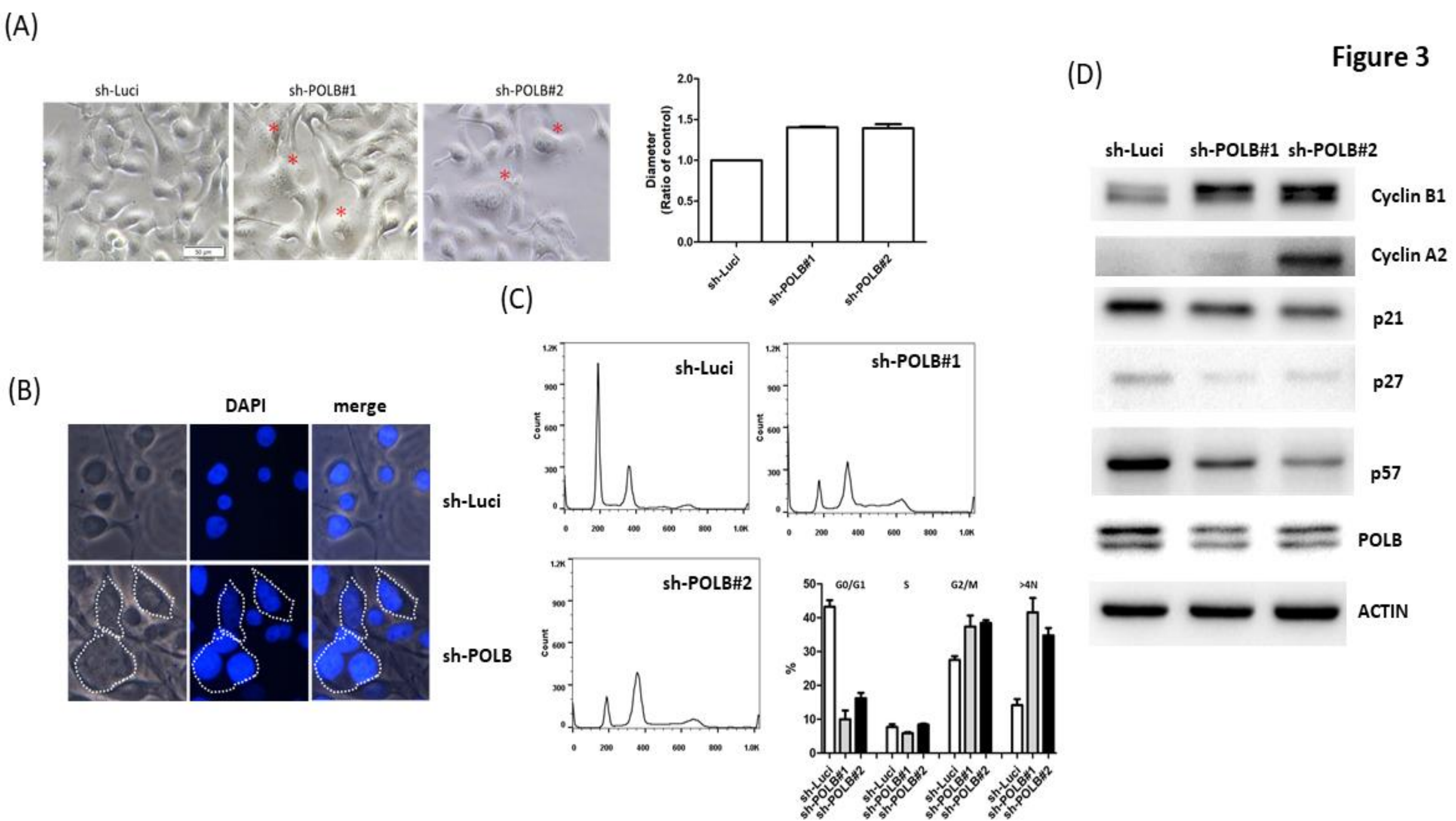
Table 2. Relationship between POLB expression and clinicopathological characteristics of oral cancer patients ($n = 133$). Statistical analysis was performed using the Chi-squared test.

Parameters	n	POLB Expression, n (%)		p-Value
		Low	High	
Total	133	63 (47.37)	70 (52.63)	
Age				
≤40 yrs	5	4 (6.35)	1 (1.43)	0.1893
>40 yrs	128	59 (93.65)	69 (98.57)	
Gender				
female	8	0 (0.00)	8 (11.43)	0.0068 *
male	125	63 (100.00)	62 (88.57)	
Tumor size				
≤2.0 cm	65	26 (41.27)	39 (55.71)	0.0961
>2.0 cm	68	37 (58.73)	31 (44.29)	
Grade				
I	59	26 (41.94)	33 (47.14)	0.6009
II/III	73	36 (58.06)	37 (52.86)	
Tumor stage				
T1/T2	101	42 (66.67)	59 (84.29)	0.0176 *
T3/T4	32	21 (33.33)	11 (15.71)	
Nodal stage				
N0	100	46 (73.02)	54 (77.14)	0.5822
N1/N2/N3	33	17 (26.98)	16 (22.86)	
Metastatic stage				
M0	132	63 (100.00)	69 (98.57)	0.3410
M1	1	0 (0.00)	1 (1.43)	
Tumor metastasis				
Absent	123	56 (88.89)	67 (95.1)	0.1907
Present	10	7 (11.11)	3 (4.29)	
Tumor recurrent				
Absent	82	34 (54.84)	48 (68.57)	0.1045
Present	50	28 (45.16)	22 (31.43)	
Survival status				
Survival	98	41 (65.08)	57 (81.43)	0.0325 *
Death	35	22 (34.92)	13 (18.57)	
Alcohol				
N	48	23 (36.51)	25 (35.71)	0.9242
Y	85	40 (63.49)	45 (64.29)	
Areca nuts				
N	31	15 (23.81)	16 (22.86)	0.8968
Y	102	48 (76.19)	54 (77.14)	
Smoking				
N	21	13 (20.63)	8 (11.43)	0.146
Y	112	50 (79.37)	62 (88.57)	

Table 3. Univariate and multivariate logistic analysis of clinicopathological independent prognostic factors for survival of oral cancer patients ($n = 133$). Statistical analysis was performed using Cox multivariate analysis.

Factors	Univariate		Multivariate	
	HR (95% CI)	p-Value	HR (95% CI)	p-Value
POLB expression		0.0688		0.0360 *
Low	1.0		1.0	
High	0.526 (0.263–1.051)		0.464 (0.226–0.951)	
Tumor Size		0.0055 *		0.1436
≤2.0 cm	1.0		1.0	
>2.0 cm	2.945 (1.373–6.315)		1.846 (0.812–4.198)	
Grade		0.0081 *		0.1823
I	1.0		1.0	
II/III	0.356 (0.166–0.765)		0.578 (0.259–1.293)	
Nodal stage		0.0002 *		0.0065 *
N0	1.0		1.0	
N1/N2/N3	3.534 (1.799–6.942)		2.777 (1.330–5.796)	
Alcohol		0.0688		0.3797
N	1.0		1.0	
Y	2.164 (0.942–4.969)		1.620 (0.552–4.750)	
Areca nut		0.3419		0.0365 *
N	1.0		1.0	
Y	0.699 (0.334–1.462)		0.413 (0.181–0.946)	
Smoking		0.2833		0.4950
N	1.0		1.0	
Y	1.913 (0.585–6.260)		1.678 (0.380–7.413)	

* Statistically significant ($p < 0.05$).



COI: The authors have no conflicts of interest to disclose