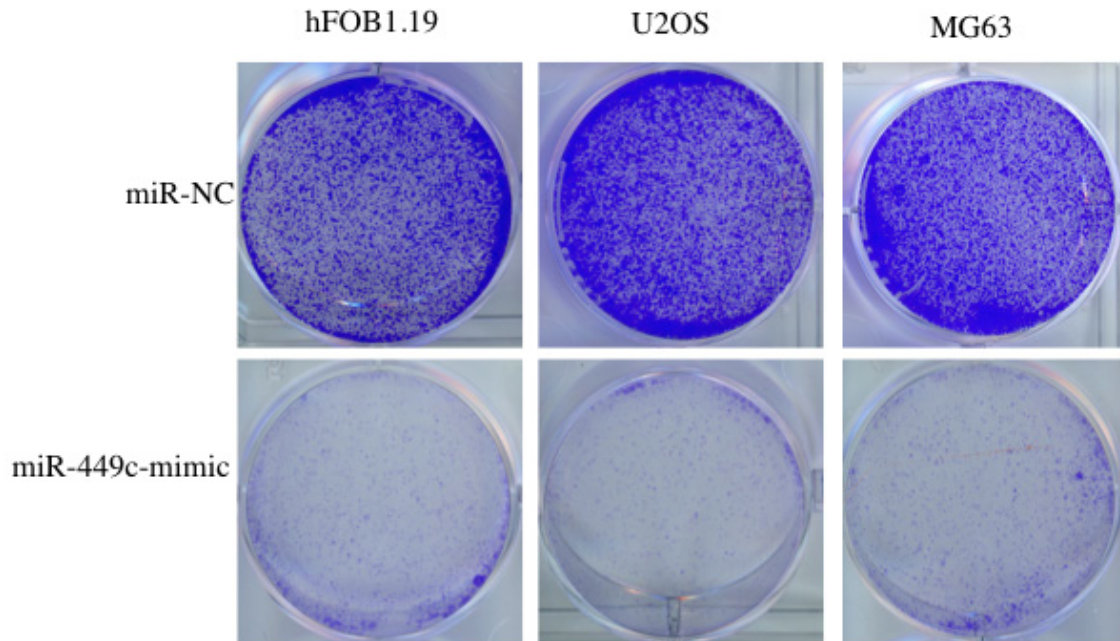**Supplementary Figure 1**

Supplementary Figure 1. Ectopic expression of miR-449c decreased osteosarcoma cell colony formation ability.

For 24 h, miR-449c-mimic and its negative control miR-NC were transfected into hFOB1.19, U2OS and MG63 cells. The transfected cells were then seeded onto 6-well plates with a density of 1×10^3 cells per well and cultured with 0.1 ml DMEM medium for two weeks. Then, cells were stained with 0.5% crystal violet and washed five times with ddH2O to remove the excess dye. Finally, pictures were taken.
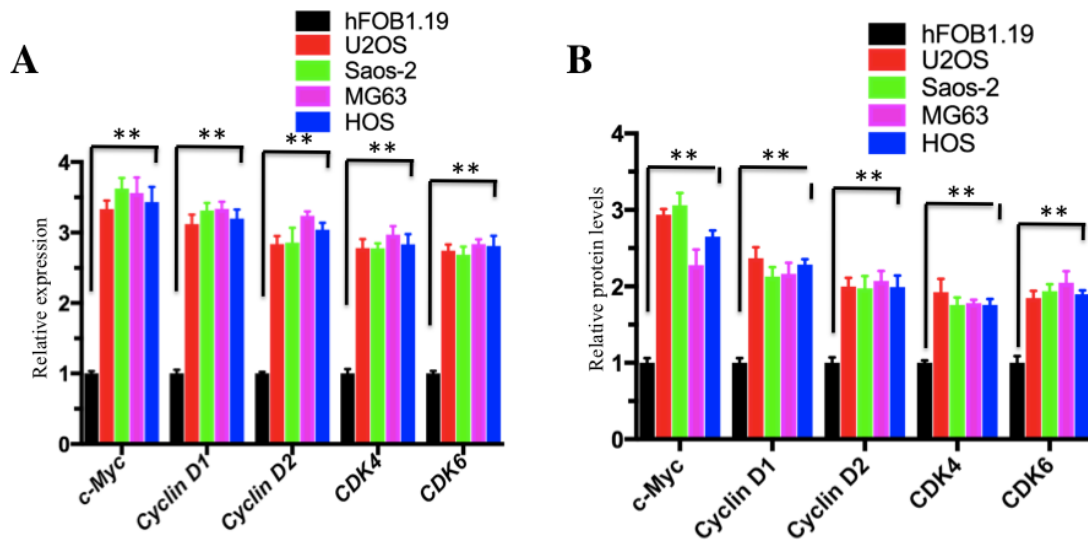
Supplementary Figure 2

A
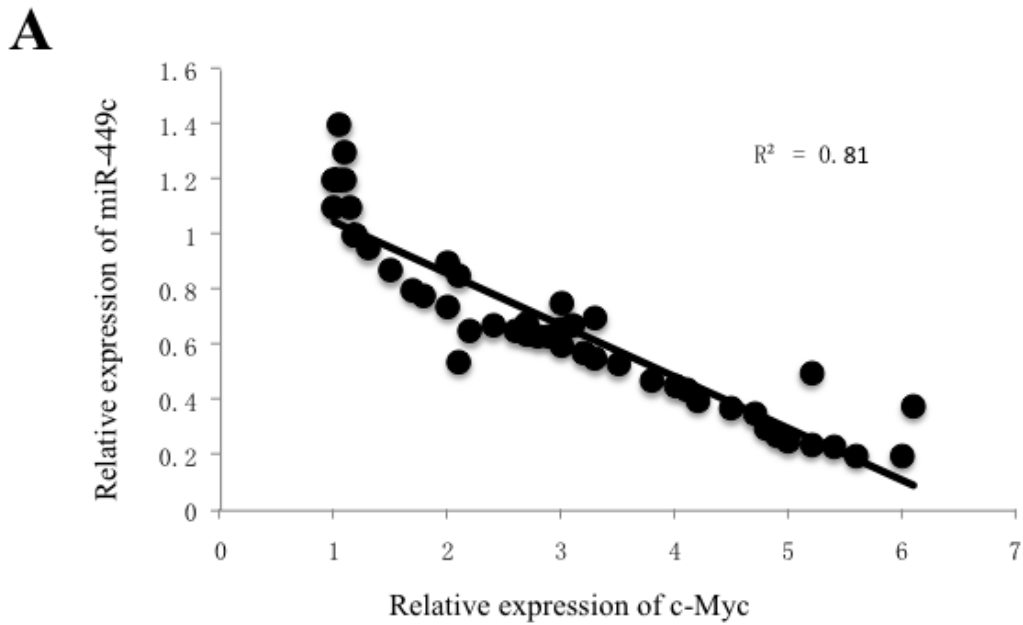
B

Correlations

		miR449	cMyc
miR449	Pearson Correlation	1	-.904[**]
	Sig. (2-tailed)		.000
	N	48	48
cMyc	Pearson Correlation	-.904[**]	1
	Sig. (2-tailed)	.000	
	N	48	48

[**]. Correlation is significant at the 0.01 level (2-tailed).

Supplementary Figure 2. Expression of *c-Myc* is negatively correlated with miR-449c expression.

The relative expression of *c-Myc* and miR-449c in in osteosarcoma tumors (n = 48) was subjected to Pearson's correlation analysis. Regression analysis demonstrated a coefficient of determination (r^2) of 0.81 **(A),** and a Pearson correlation coefficient (r) of 0.904 ($P <$ 0.001) **(B)**. Each point represents one gene pair.
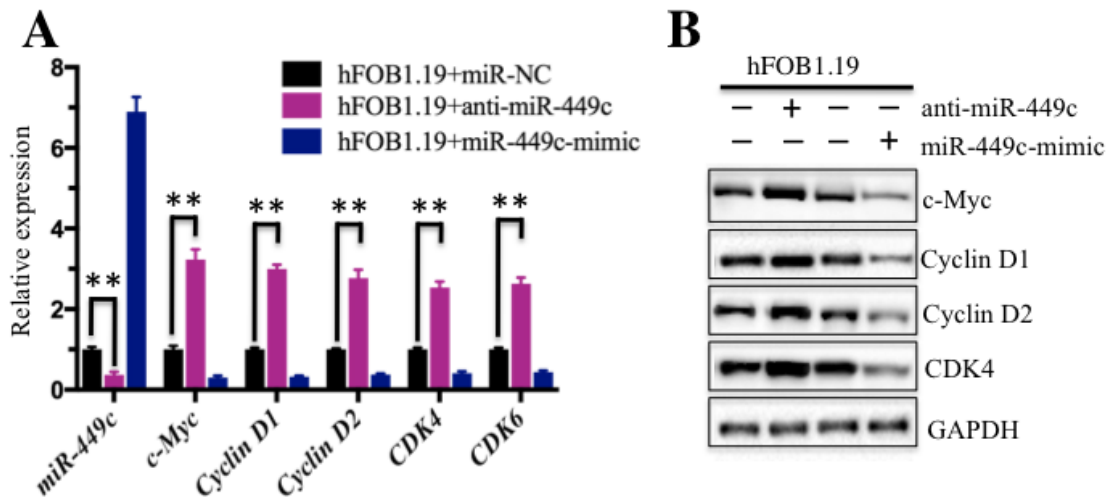
Supplementary Figure 3

Supplementary Figure 3. Relative mRNA and protein levels of cell cycle regulators in osteosarcoma cells.

(A) The mRNA levels of cell cycle regulators were decreased in osteosarcoma cells. The mRNAs from hFOB1.19, U2OS, Saos-2, MG63, and HOS cells were subjected to qRT-PCR analyses to determine the expression of *c-Myc*, *Cyclin D1*, *D2*, *CDK4* and *CDK6*. Expression was normalized to *GAPDH* in each cell line, and the resulting ratios in hFOB1.19 cells were arbitrarily defined as 1-fold. **(B)** The protein levels of cell cycle regulators were decreased in osteosarcoma cells. Statistical analysis of the protein levels are shown in Figure 3F. Representative data from three independent experiments are shown. **$P < 0.001$.
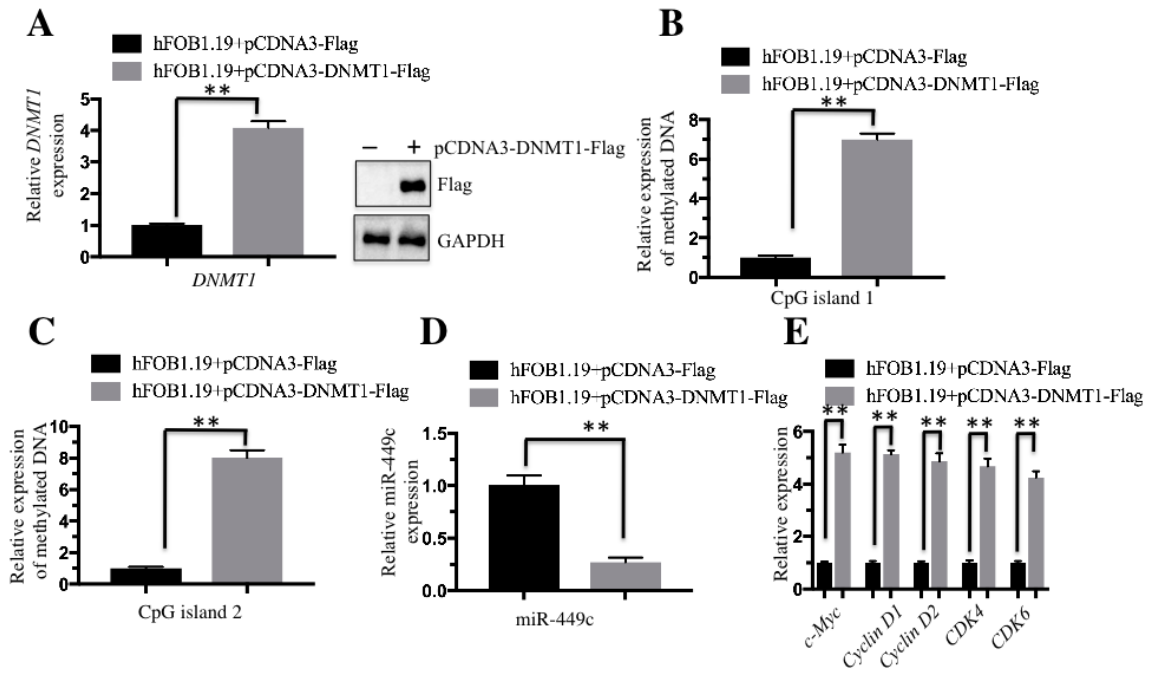
Supplementary Figure 4

Supplementary Figure 4. Repression of miR-449c resulted in upregulation of c-Myc in hFOB1.19 cells.

The hFOB1.19 cells were transfected with miR-NC, anti-miR-449c, or miR-449c-mimic, respectively. After 48 h, multiple studies were performed: miR-449c expression and mRNA levels of cell cycle regulators including c-Myc, Cyclin D1, D2, CDK4 and CDK6 **(A)**, protein levels of these same regulators **(B)**. Representative data from three independent experiments are shown. **$P < 0.001$.

Supplementary Figure 5

Supplementary Figure 5. Overexpression of *DNMT1* resulted in downregulation of miR-449c in hFOB1.19 cells.

The hFOB1.19 cells were transfected with pCDNA3-DNMT1-Flag plasmid. After 48 h, cells were collected and subjected to multiple studies including examination of DNMT mRNA and protein levels **(A)**, detection of methylated CpG islands **(B** and **C)**, detection of miR-449c expression **(D)**, as well as examination of mRNA levels of cell cycle regulators including c-Myc, Cyclin D1, D2, CDK4 and CDK6 **(E)**. Representative data from three independent experiments are shown. **$P < 0.001$.

Supplementary Table-1. Expression levels of miR-449c and different clinicopathological futures in patients with OS

Characteristics	Number of cases	Relative expression of miR-449c		
		Low (<1-fold)	High (≥1-fold)	*P*-value
Gender				
Male	20	17	3	0.404
Female	28	21	7	
Age				
≥20	15	13	2	0.440
<20	33	27	8	
Tumor size				
≥12 cm	10	10	0	0.0003**
<12	38	28	10	
MSTS stages				
I	12	2	10	0.0001**
II/III/IV	36	36	0	

*P < 0.05, **P < 0.001

Supplementary Table-2. Primers used for qRT-PCR

Gene	Forward	Reverse
GAPDH	5'- AATCCCATCACCATCTTCCA-3'	5'- TGGACTCCACGACGTACTCA-3'
c-Myc	5'-CTTGAACAGCTACGGAACTC -3'	5'-GAGGCAGTTTACATTATGGC-3'
CCND1	5'-TGAAGCCAGCTCACAGTGCT -3'	5'-AGCCAGGATGGTTGAGGTAA-3'
CCND2	5'-AGTGTGATGCCATATCAAGT -3'	5'-ACACTGAACAGATAAGACCT-3'
CDK4	5'-CTCTACACTAAGGGGTATGT-3'	5'-GCTCCACTGACTTCCTAGGC-3'
CDK6	5'-CTGTTGCAGTGGCAAAGGTA-3'	5'-CATAAGTGAACACATTGGAC-3'

Supplementary Table-3. Primers used for qMSP

Gene	Forward	Reverse
GAPDH	5'- CGCTTTCTTTCCTTTCGC-3'	5'- TGCCCATTCATTTCCTTCC-3'
Island 1	5'-TTTGGTTTTAAATAGATATTATG -3'	5'-CAAAACTAACTTAAACCTAAAAAA-3'
Island 2	5'-TTGGGAGTAGTTAGGTTTTTTTA -3'	5'-ACCCATCTAATTCCCTATCATTTC-3'