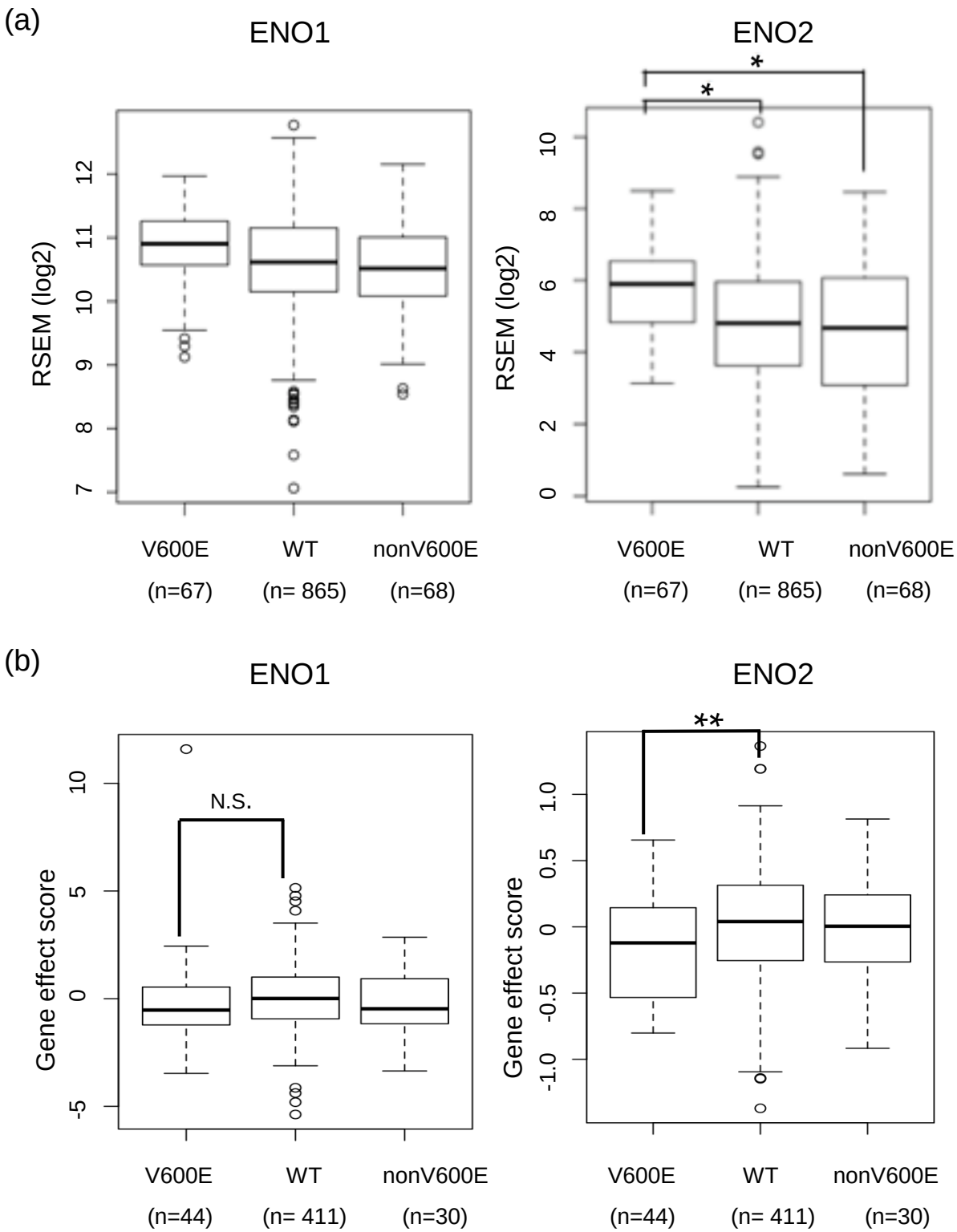
Supplementary Fig. S1

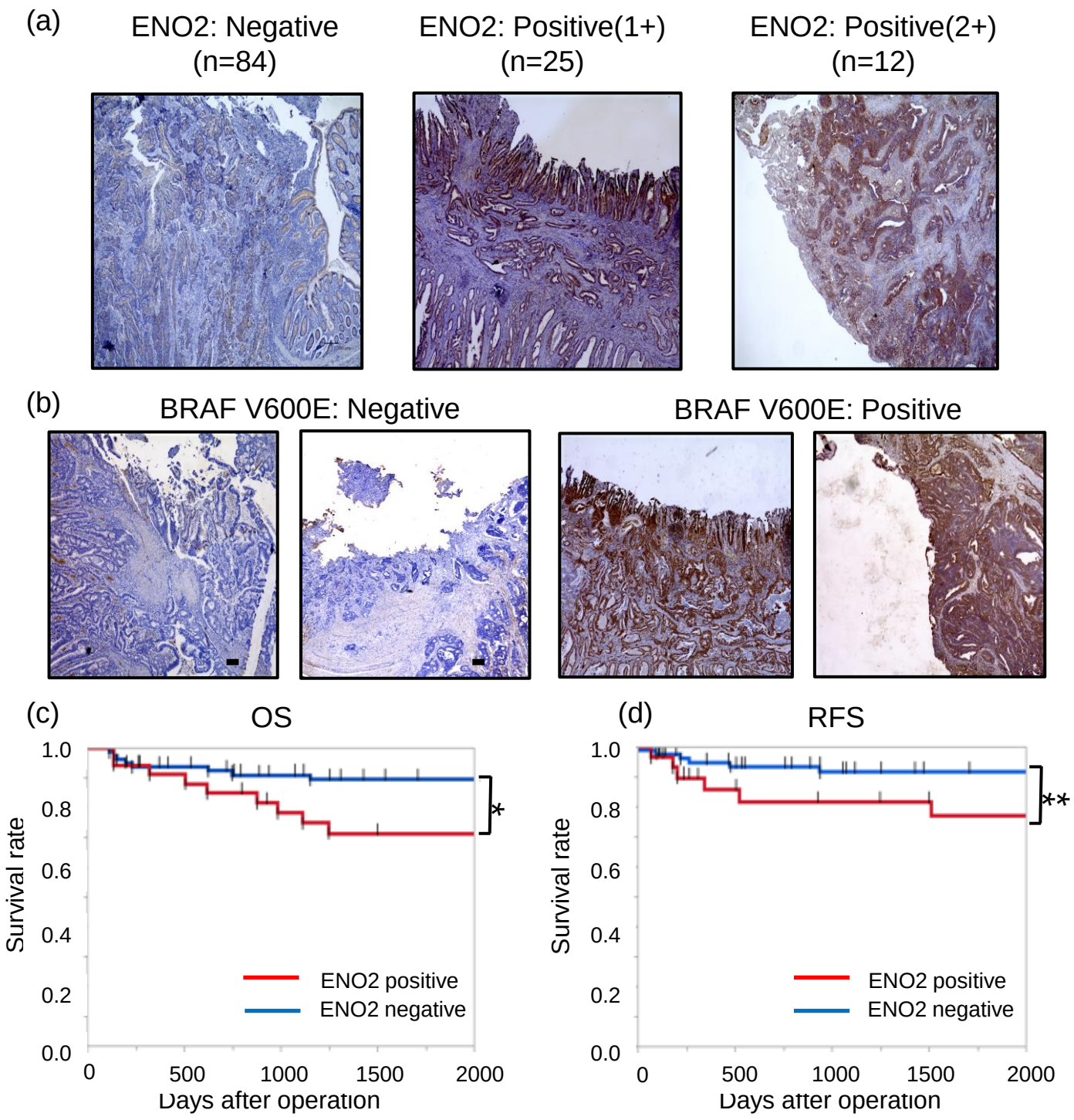


Supplementary Fig. S1. Expression analysis of ENO1 and ENO2 in cell lines

(a) Expression levels of ENO1 and ENO2 according to BRAF mutation status in Cancer Cell Line Encyclopedia (CCLE) database (*p < 0.0001). CCLE (portals. Broadinstitute.org/ccle).

(b) Gene effect scores of ENO1 and ENO2 accoring to BRAF mutation status in Project Achilles database (N.S., not significant : **p < 0.05). Project Achilles (depmap.org/portal/achilles/)

Supplementary Fig. S2



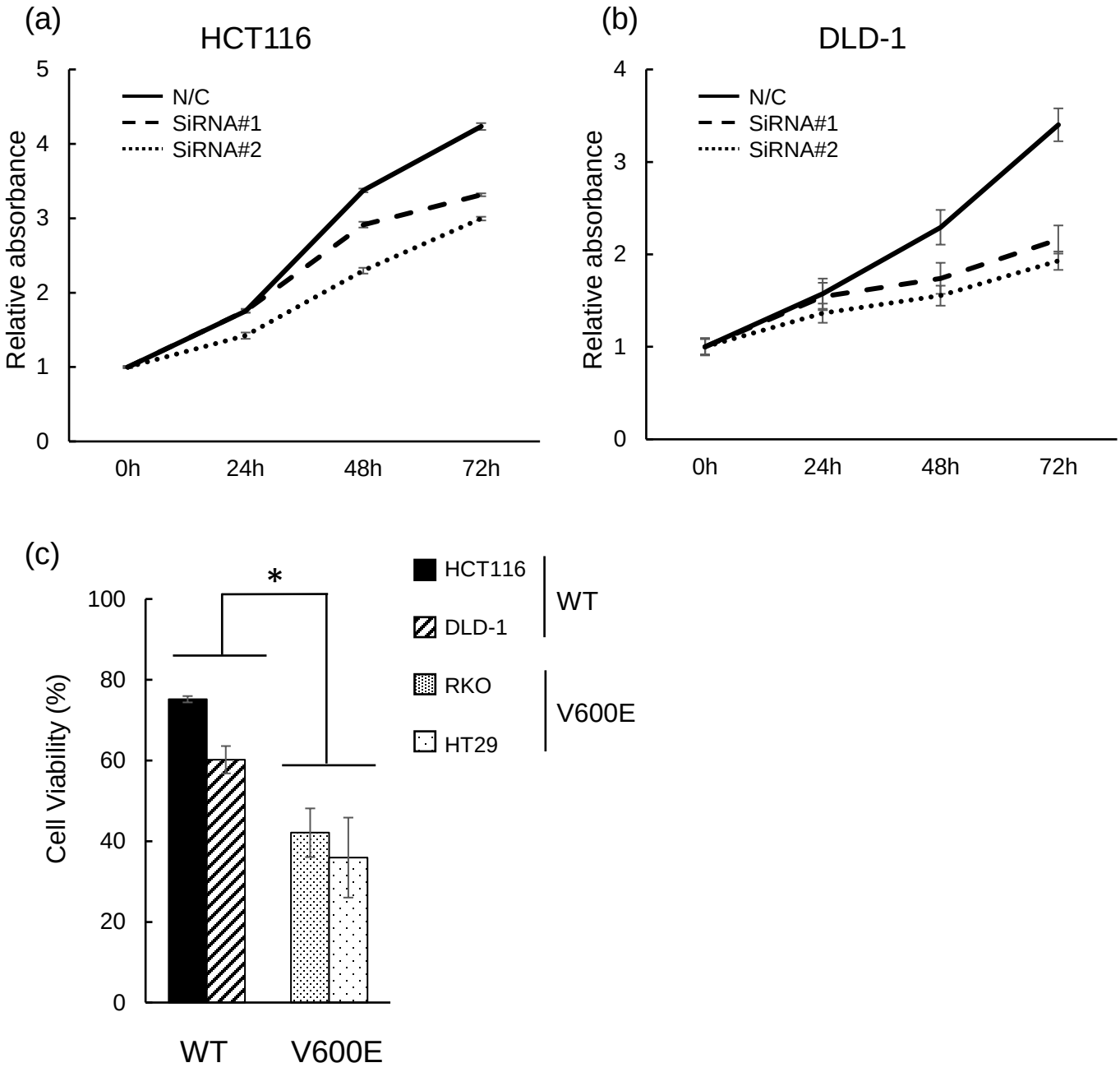
Supplementary Fig. S2. Immunohistochemical analysis of ENO2 and its prognostic impact in CRC

(a) Representative images of immunohistochemical staining using anti-ENO2 antibody. Examples of strong, weak and negative intensity are presented. Scale bar: 50 μm. Strong and weak staining were defined as ENO2-positive group.

(b) Representative images of immunohistochemical staining using anti-BRAV600E antibody. Examples of positive and negative intensity are presented. Scale bar: 50 μm.

(c,d) Kaplan–Meier curves for (c) overall survival and (d) relapse-free survival, according to ENO2 expression status in patients with CRC.

Supplementary Fig. S3



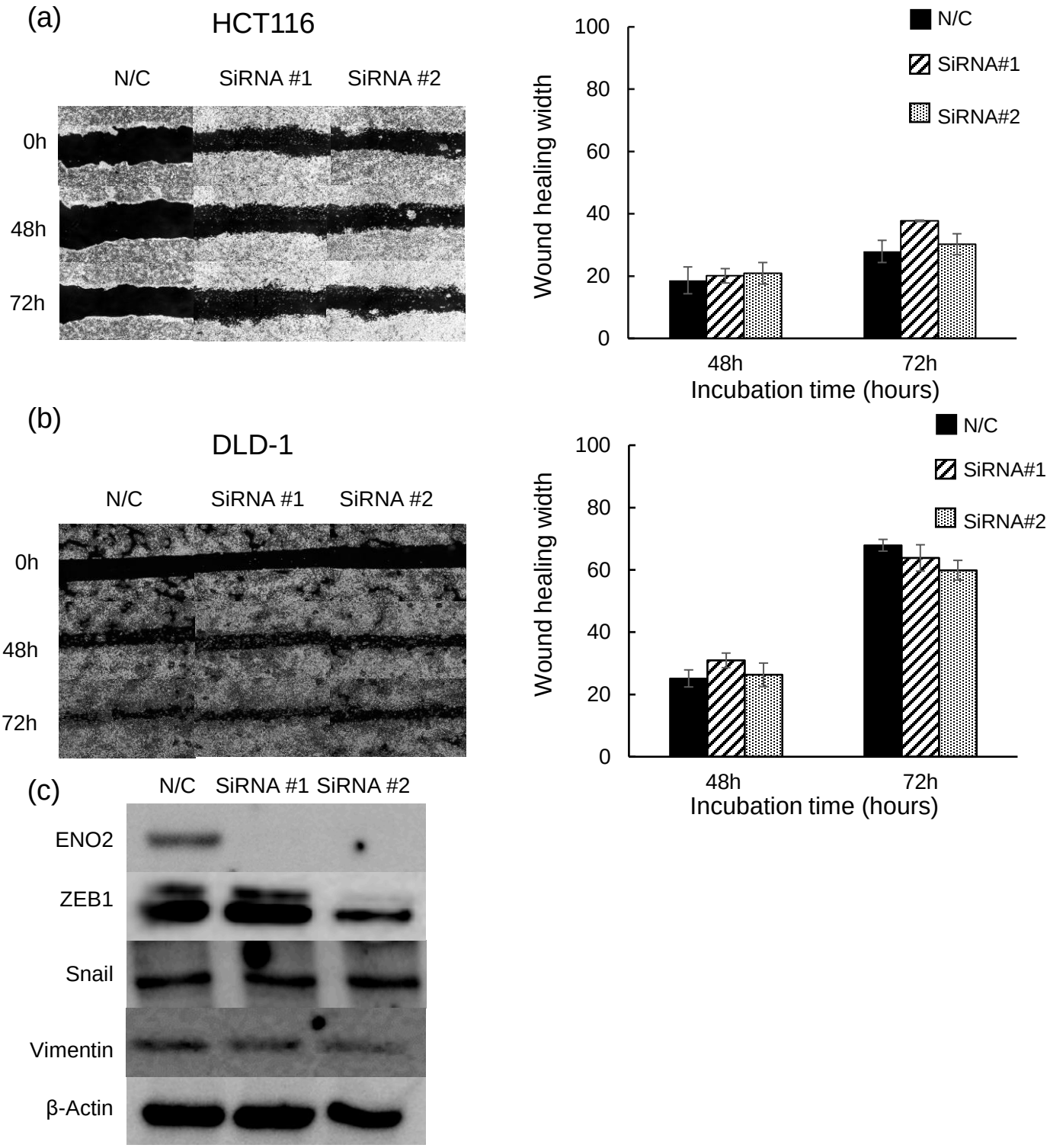
Supplementary Fig. S3. Impact of ENO2 knockdown on proliferation of BRAF wild-type CRC cells

(a) Proliferation assay after transfection with N/C or ENO2 siRNAs in HCT116.

(b) Proliferation assay after transfection with N/C or ENO2 siRNAs in DLD1.

(c) Bar plots showing the cell viability of CRC cells in 72h after transfection in CRC cell lines. HCT116 (BRAF wild-type), DLD-1 (BRAF wild-type), RKO (BRAF V600E-mutated), and HT29 (BRAF V600E-mutated) with the siRNAs. *p<0.05

Supplementary Fig. S4



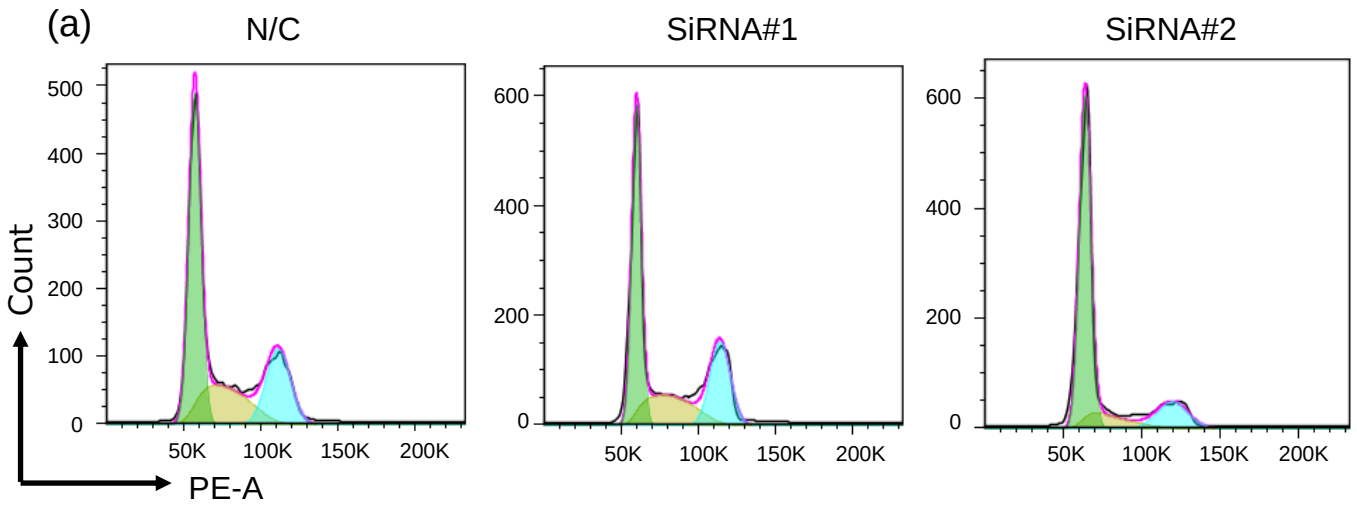
Supplementary Fig. S4. Impact of ENO2 knockdown on BRAF wild-type CRC cell.

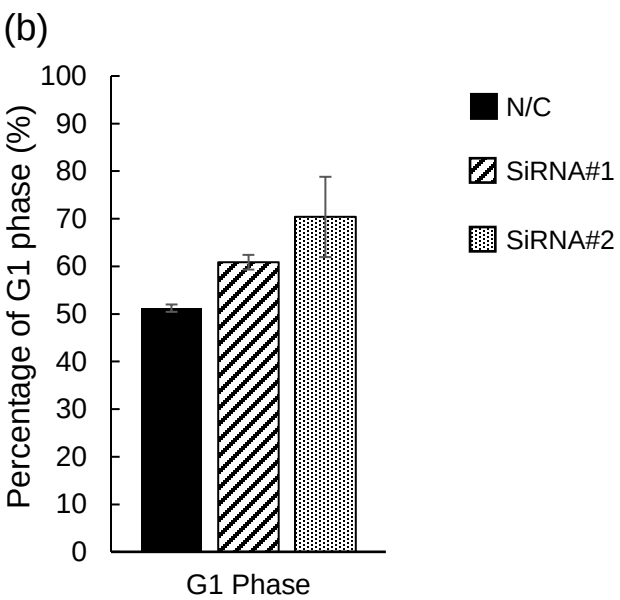
(a) (left) Representative picuters of scratch wound healing assay of HCT116 cells transfected with N/C or ENO2 siRNAs. Magnification: x100.
(right) Average distance between wound edges for 5 different areas at the indicated time points (relative change from the distance at 0 h). Each bar presents the mean ± SEM of triplicate measurements (*p < 0.05).

(b) (left) Representative picutres of scratch wound healing assay of DLD-1 cells transfected with N/C or ENO2 siRNAs. Magnification: x100.
(right) Average distance between wound edges for 5 different areas at the indicated time points (relative change from the distance at 0 h). Each bar presents the mean ± SEM of triplicate measurements (*p < 0.05).

(c) Epithelial mesenchymal transition (EMT) related protein expression levels in RKO cells transfected with N/C and ENO2 siRNAs (siRNA#1 and siRNA#2) in western blot analysis.

Supplementary Fig. S5



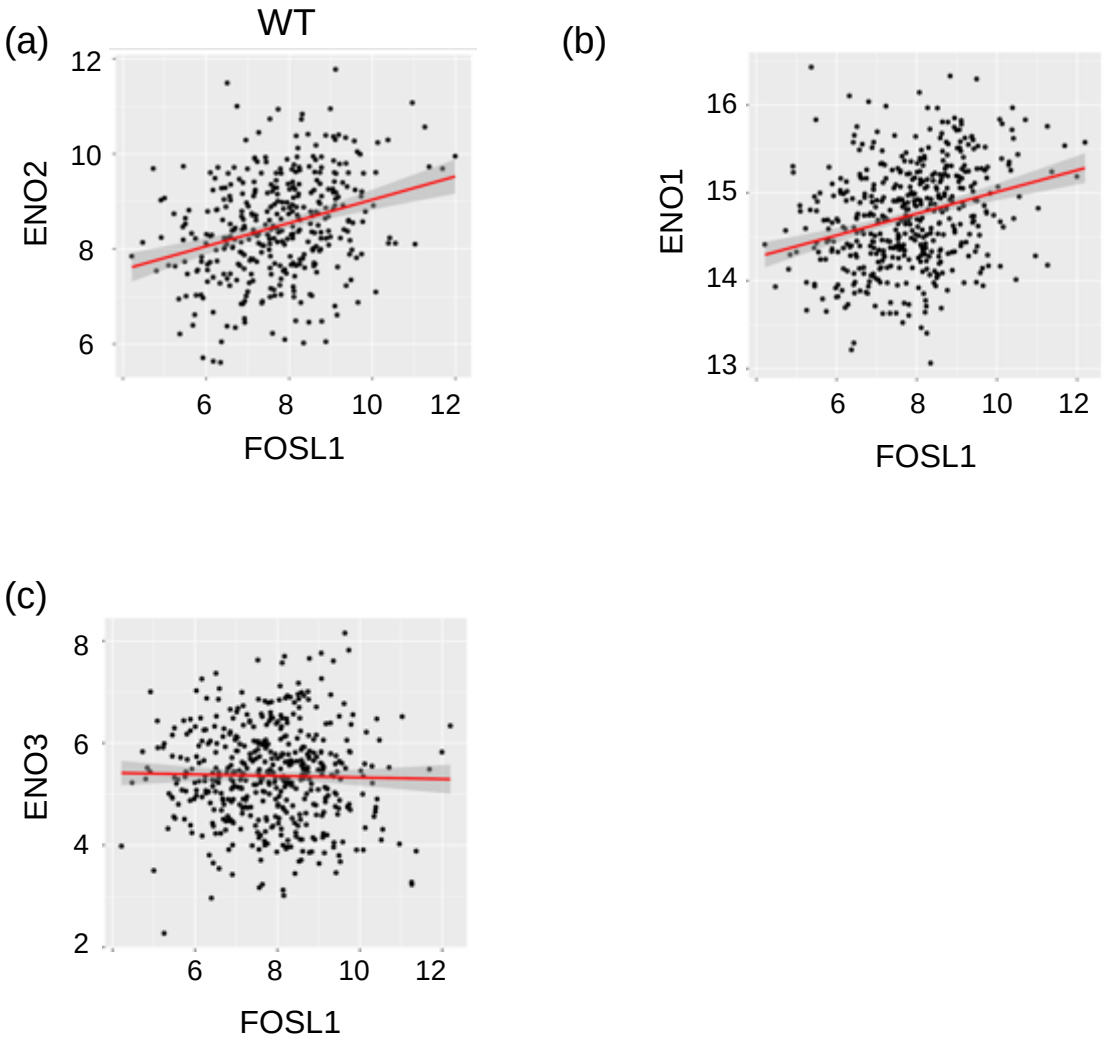


Supplementary Fig. S5. Impact of ENO2 knockdown on cell cycle progression in BRAF V600-mutated CRC cells

(a) Histogram showing cell cycle analysis in RKO cells transfected with N/C or ENO2 siRNAs.

(b) Proportion of cells in G1 phase.

Supplementary Fig. S6



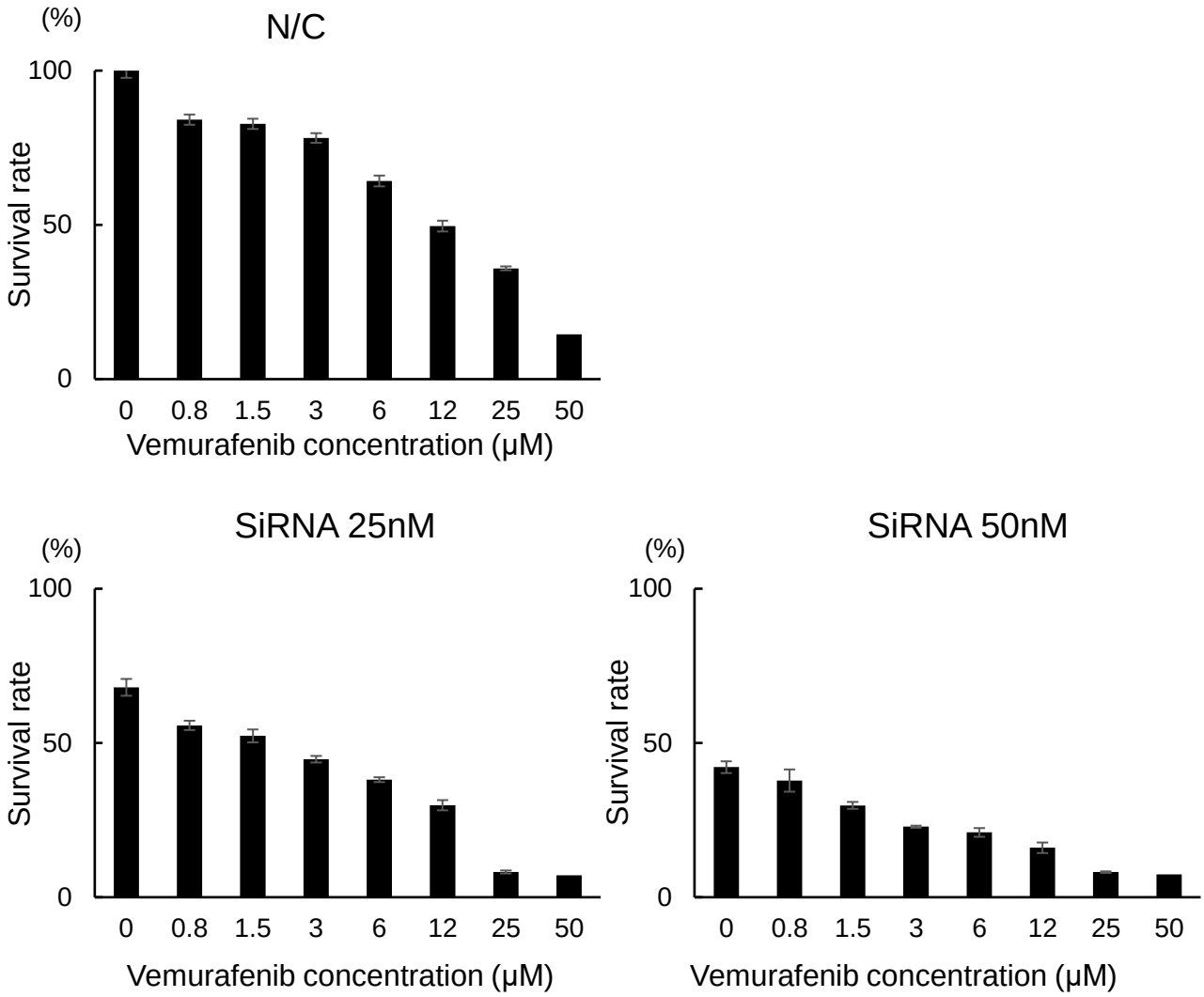
Supplementary Fig. S6. Correlation between ENO2 and FOSL1 expression according to BRAF mutation status

(a) Correlation between ENO2 and FOSL1 expression in BRAF wild type (n= 373, r=0.30, p=5.48e-09)

(b) Correlation between ENO1 and FOSL1 expression (n=481, r= 0.29, p= 1.59e-10)

(c) Correlation between ENO3 and FOSL1 expression (n=481, r= -0.22, p= 0.63)

Supplementary Fig. S7



Supplementary Fig. S7. Rate of Viable cell numbers at each vemurafenib concentrations divided by cell numbers with negative control SiRNA and without vemurafenib exposure as 100%