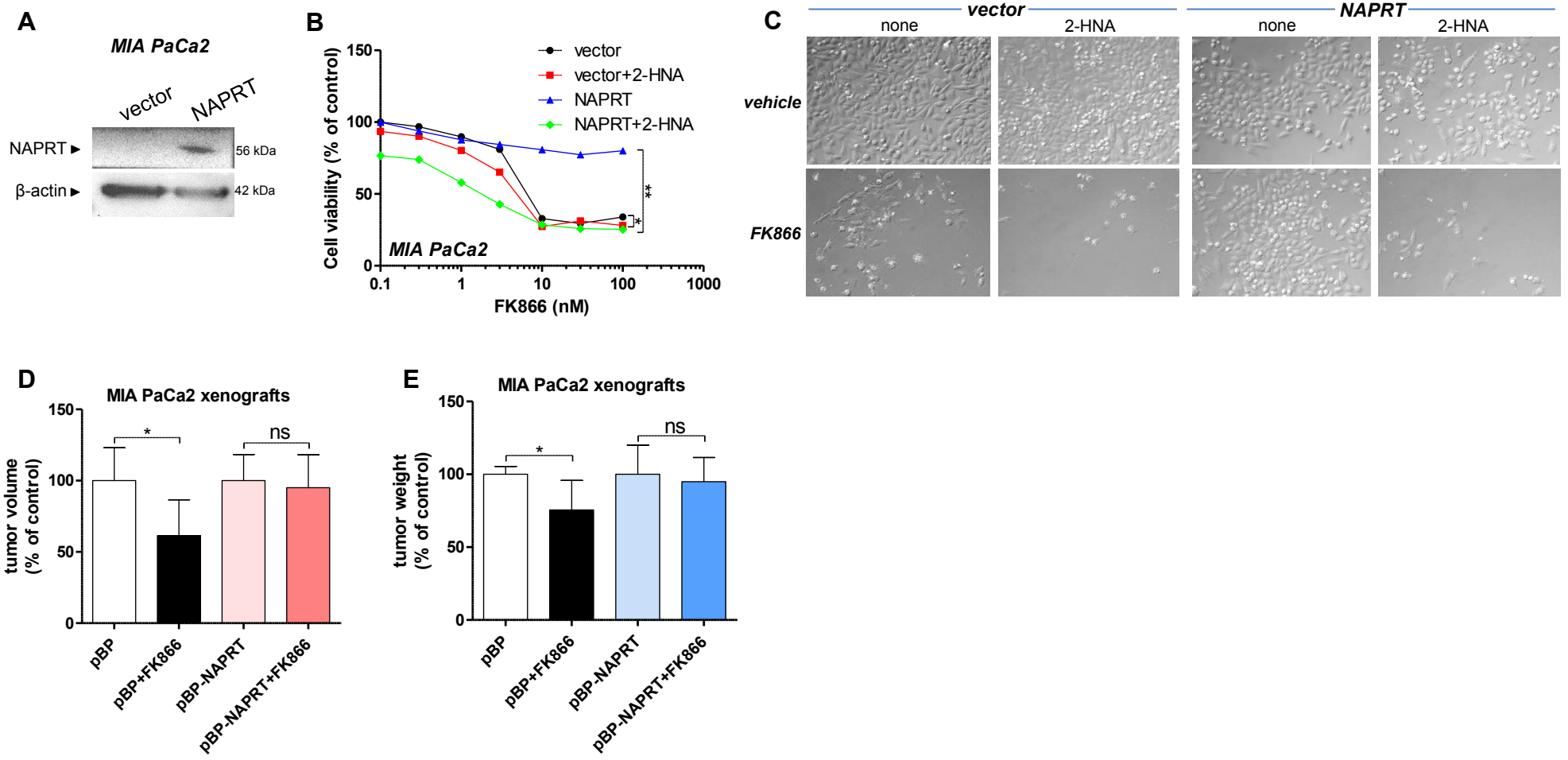

Figure S6. NAPRT overexpression confers resistance to FK866 to MIA PaCa2 cells, but resistance is reverted by 2-HNA. A, MIA PaCa2 cells were retrovirally engineered to overexpress NAPRT or a control vector (pBABEpuro). Thereafter, cells were used for protein lysate generation and NAPRT and β-actin levels were detected by immunoblotting. B, C, 2 x 10^3 MIA PaCa2 cells expressing NAPRT or a control vector were plated in each well of 96-well plates, allowed to adhere overnight and then incubated for 72 h w/ or w/o FK866 at the indicated concentrations in the presence or absence of 1 mM 2-HNA. Thereafter, cell viability was detected with SRB (B) after cell imaging by light microscopy (C). D, E, 3,5 x 10^6 MIA PaCa2 cells engineered to express the vector pBP or pBP-NAPRT were injected subcutaneously into nude mice. When the tumors appeared as established palpable masses, mice (n=6 per treatment arm) were randomly assigned to receive either vehicle or FK866 for three weeks. At the end of the experiment, tumor volume and tumor weight were determined. In control (pBP) MIA PaCa2 xenografts, FK866 reduced tumor volume by 39% and tumor weight by 24%. A, C, One representative experiment out of three is presented. B, Data are presented as means of three separate experiments. In panel B, the statistical analysis refers to the experimental values obtained with 100 nM FK866. ns: non-significant; *: $p<0.05$; **: $p<0.01$.