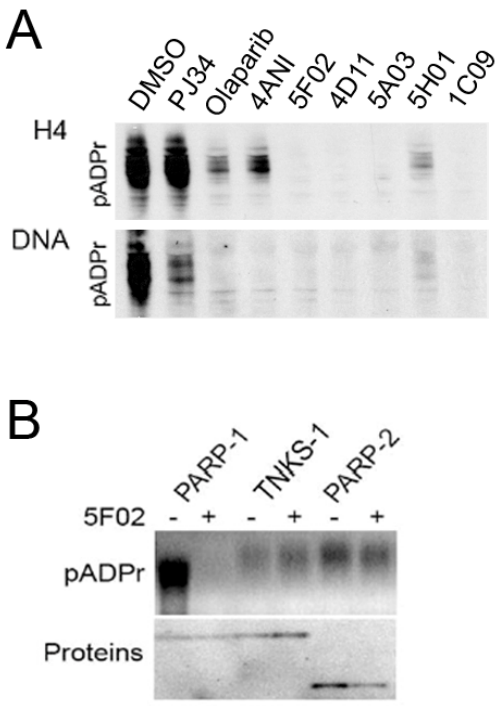
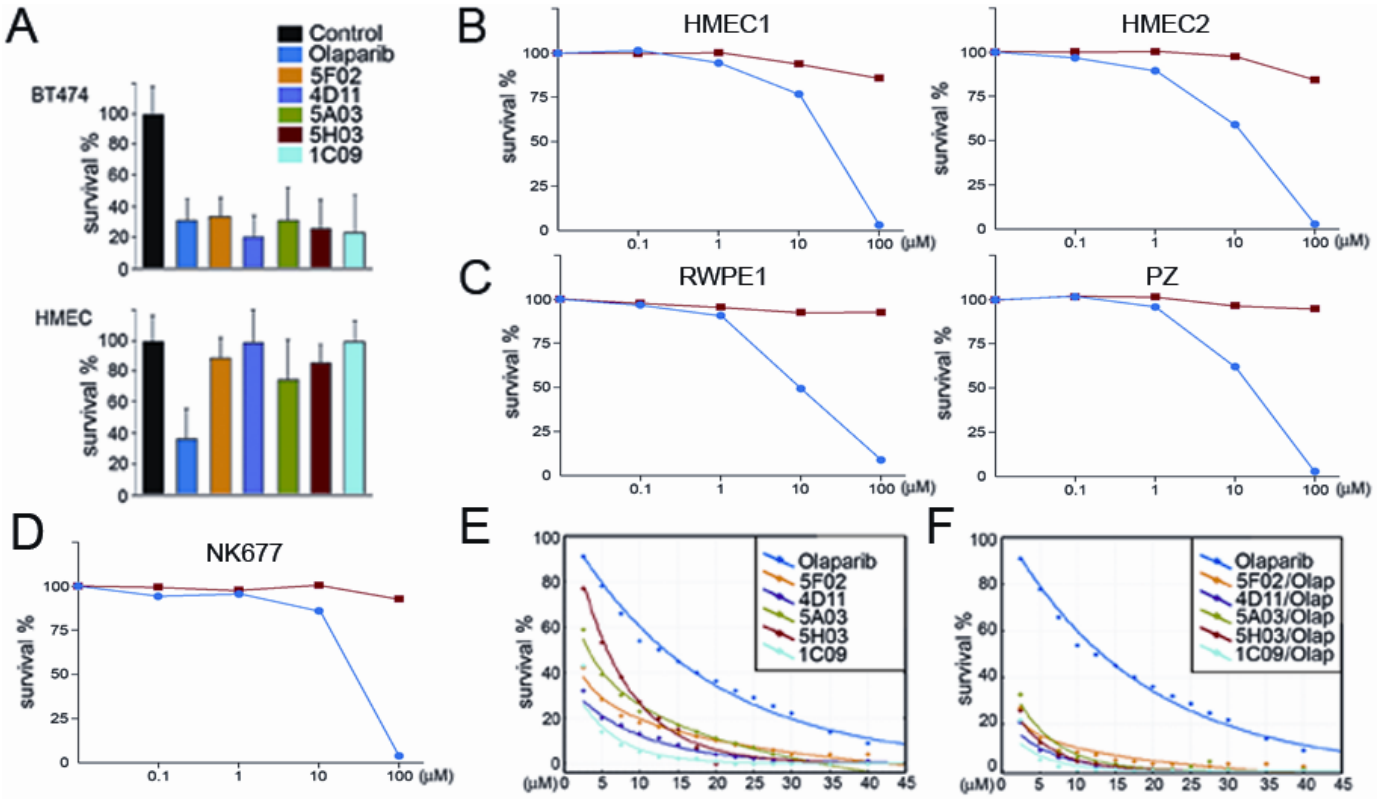


Supplemental Figure S1. New non-NAD-like inhibitors are specific toward PARP-1 inhibition. (**A**) PARP-1 *in vitro* activation assays by H4 and DNA. New non-NAD-like inhibitors (5F02,4D11,5A03,5H01,1C09) block DNA- and histone-dependent PARP-1 activation *in vitro*. PJ34, Olaparib and 4ANI are NAD-mimicking PARP-1 inhibitors. All inhibitors were used in 5mkM concentration. (**B**) The new PARP-1 inhibitor 5F02 (5mkM) suppresses PARP-1, but not Tankyrase-1 or PARP-2.



Supplemental Figure S2. Tumor cell suppression by classical NAD-mimetic and novel non-NAD-like PARP-1 inhibitors. (**A**) Non-NAD-like inhibitors specifically suppressed the proliferation of breast cancer-derived cells (BT174) with no cytotoxicity to normal cells. The upper graph shows the survival rate of breast cancer-derived cells (BT474) after treatment with Control (DMSO), Olaparib and non-NAD-like inhibitors. Normal cells (HMEC) and breast cancer-derived cells (BT474) were plated at a density of 10^4 cells/well (100 µl) in a 96-well plate. On the next day, Olaparib, a NAD-mimetic, or new non-NAD-like inhibitors (5F02,4D11,5A03,5H03,1C09) were added (5 µM). Control cells were grown with DMSO solution added. Cells were grown for 72 hours. Twenty µl/well of Alamar Blue Reagent were added; fluorescence readings were taken. The lower graph shows that Olaparib suppressed the proliferation of normal (HMEC) cells, while non-NAD-like inhibitors eliminated cancer cells with no cytotoxicity to normal cells. Olaparib suppressed both normal and cancer cells. New non-NAD-like inhibitors: 5F02,4D11,5A03,5H03,1C09. *$p<0.05$ in comparison to control. (**B-D**) Normal human cells are insensitive to 5F02 treatment. Normal breast (HMEC1 and HMEC2) (**B**), prostate (RWPE1 and PZ) (**C**), and kidney (NK677) (**D**) cells were plated at a density of 10^4 cells/well (100 µl) in a 96-well plate. On the next day, increasing dose of Olaparib (blue), a NAD-mimetic, and 5F02 (red), a new non-NAD-like inhibitor, were added. Cells were grown for 72 hr, followed by staining with Alamar Blue Reagent and fluorescence reading. **5F02** had no cytotoxicity to normal cells, while **Olaparib** suppressed normal cell growth. All experiments were performed in three replicas. (**E**) New PARP-1 inhibitors suppressed the malignancy potential of PC-3 cells. (**F**) New PARP-1 inhibitors showed synergistic interaction with Olaparib. Calculation of cell survival rate in (**E,F**) was based on clonogenic cell survival assays. PC-3 cells were plated into 24-well plates. Cells were allowed to adhere overnight and were treated a non-NAD-like inhibitor (5F02, 4D11, 5A03, 5H03, 1C09) (blue), Olaparib (magenta), and both (yellow) for 14 days. Colonies were counted and plotted on the graph. Data were fitted to exponential and logarithmic decay models using nonlinear curve fitting module of Statistica 7.0 software. The best fitting models for each inhibitor are represented on the chart.