Title: Identification of DNA repair pathways that affect the survival of ovarian cancer cells treated with a PARP inhibitor in a novel drug combination

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SUPPLEMENTAL FIGURE LEGENDS

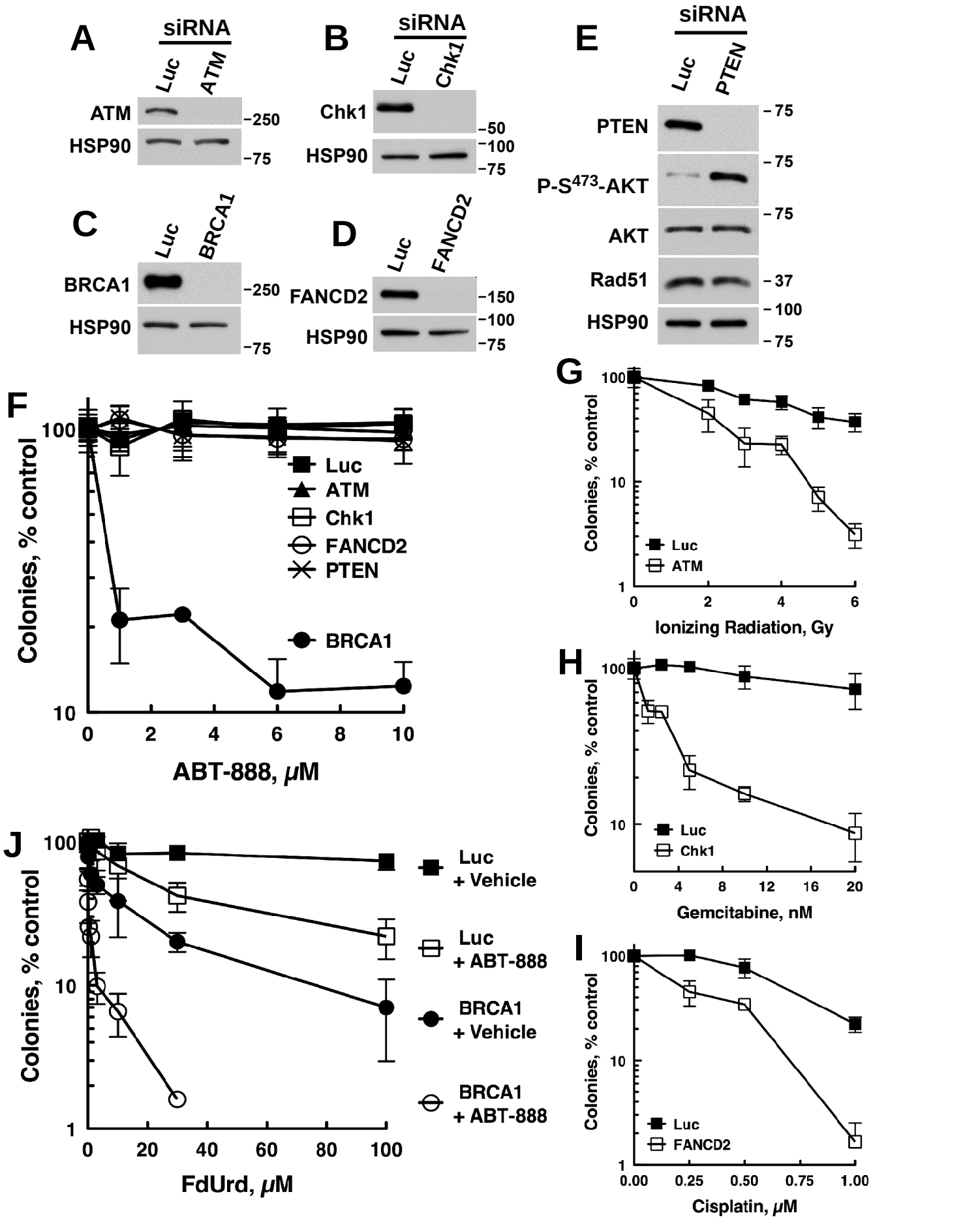
Supplemental Figure 1. Depletion of BRCA1— but not ATM, Chk1, FANCD2, or PTEN—sensitizes SKOV-3 ovarian cancer cells to ABT-888. (A-J) SKOV-3 cells were transfected with control luciferase (Luc), ATM (A), Chk1 (B), BRCA1 (C), FANCD2 (D), or PTEN (E) siRNAs. 48 h later, the cells were processed for immunoblotting (A) or for clonogenic assays, in which they were exposed to ABT-888 continuously (F) until colonies formed (8-9 d). Alternatively, the same transfected cells were exposed to ionizing radiation (G), gemcitabine for 24 h (H), cisplatin for 24 h (I), or FdUrd alone or with 3 μM ABT-888 for 24 h. Following exposure to gemcitabine, cisplatin, FdUrd alone, or F+A (FdUrd+ABT-888) the cells were washed. 3 μM ABT-888 was re-added to cells that were previously exposed to ABT-888 in (J). In (A) approximate molecular masses are given in kiloDaltons.

Supplemental Figure 2. Depletion of ATR and Chk1 sensitizes OVCAR-8 cells to gemcitabine. The same transfected cells as used in Fig. 2, were processed for clonogenic assays and then exposed to gemcitabine for 24 h, washed and cultured until colonies formed.

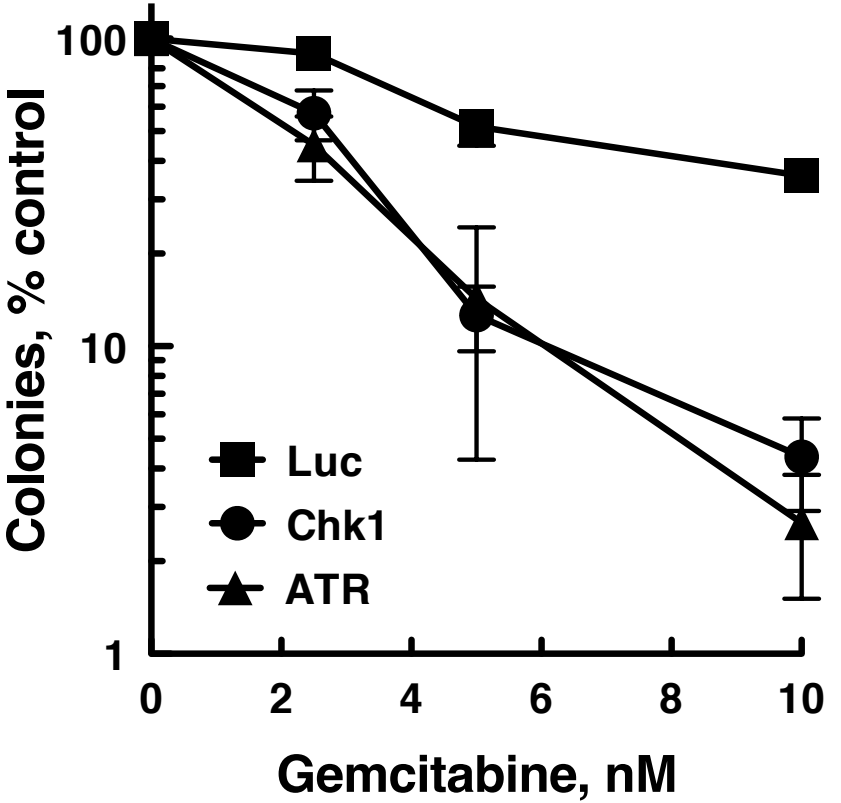
Supplemental Figure 3. Depletion of KU80, XPA, FANCD2 and RAD18 sensitizes OVCAR-8 cells to control DNA-damaging agents. (A-D) The same transfected cells as used in Figure 4 were used for clonogenic assays. Cells depleted of KU80 were exposed to ionizing radiation (A). Cells depleted of XPA were exposed to 254-nm ultraviolet light (B). Cells depleted of FANCD2 (C) or RAD18 (D) were exposed to cisplatin for 24 h, washed, and cultured until colonies formed.

Supplemental Figure 4. Depletion of KU80, FANCD2, or RAD18 does not sensitize OVCAR-8 cells to ABT-888. (A-D) the same transfected cells as used in Figure 4 and Supplemental Figure 3 were processed for clonogenic assays in which they were exposed to the indicated concentrations continuously until colonies formed. As a control, cells transfected with BRCA1 siRNA were also included in the clonogenic assays.

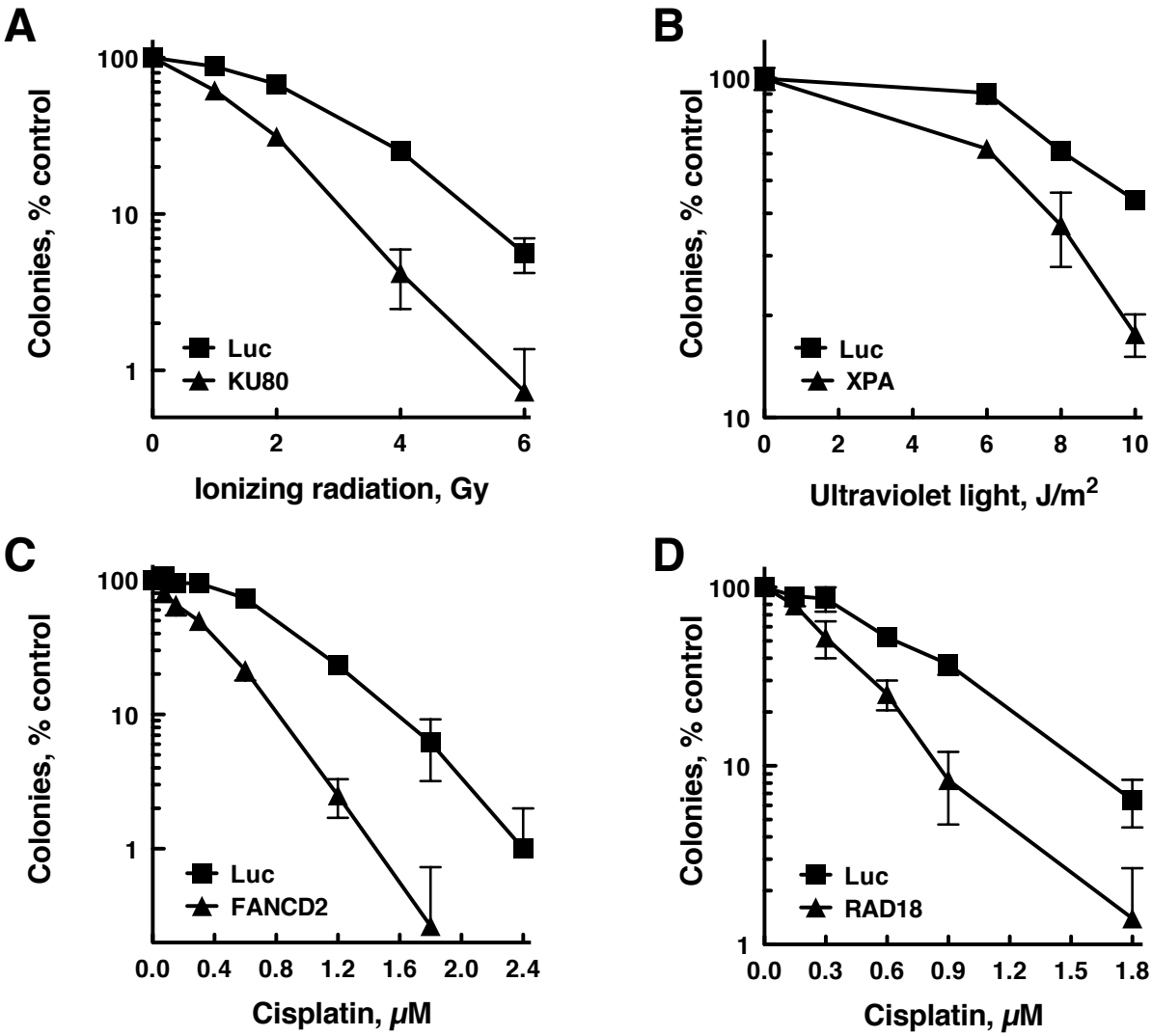
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4