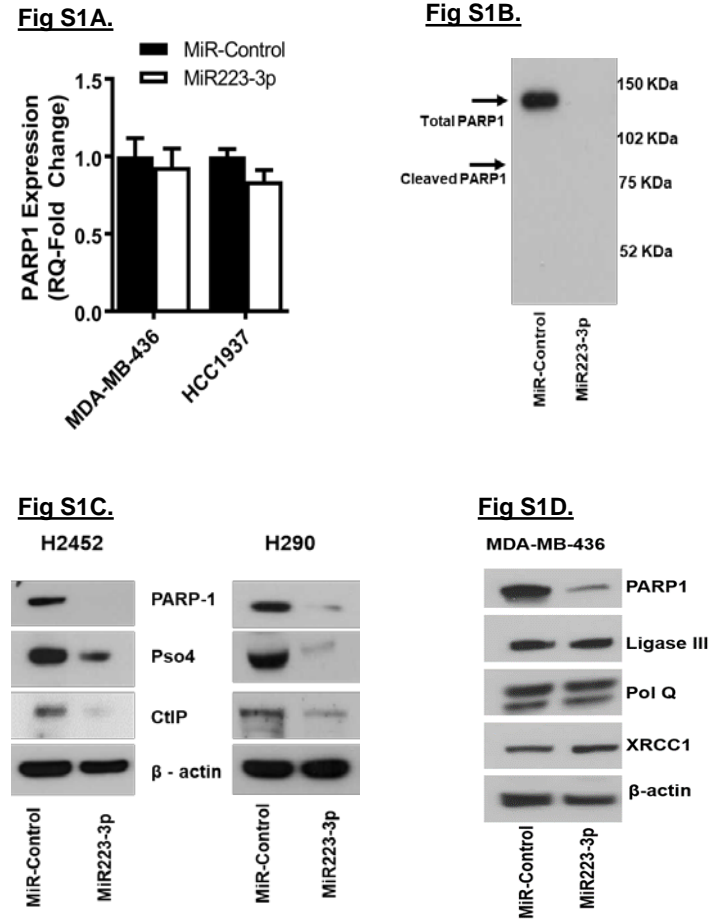


Supplementary Figures



Supplementary Figure 1. S1A. Quantitative RT-PCR (qRT-PCR) showing levels of PARP1 mRNA following transfection with miR223-3p in BRCA1-deficient MDA-MB-436 and HCC1937 breast cancer cells. **S1B.** Western blot for PARP1 and cleaved PARP following transfection with miR223-3p in MDA-MB-436 cells. Mir223-3p does not result in cleavage of PARP1. **S1C.** Western blot for PARP1, Pso4 and CtIP in H2452 and H290 cells. **S1D.** Western blot for aNHEJ components PARP1, Ligase III, PolQ and XRCC1 in MDA-MB-436 cells.

Fig S2A.

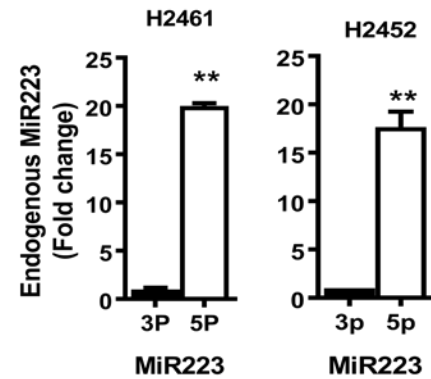


Fig S2B.

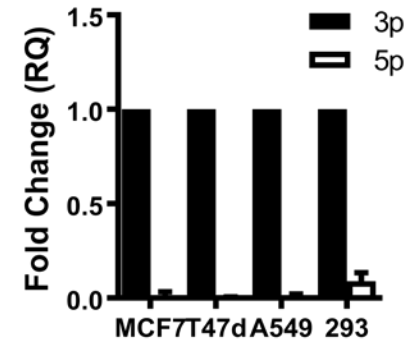


Fig S2C.

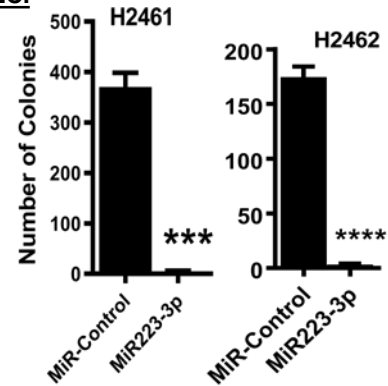
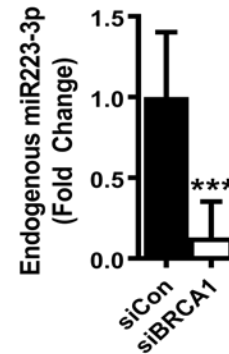


Fig S2D.



Supplementary Figure 2. S2A. qRT-PCR comparing the levels of miR223-3p and miR223-5p in BAP1-deficient malignant pleural mesothelioma cells, H2452 and H2461. **S2B.** qRT-PCR comparing the levels of miR223-3p and 5p HR-proficient MCF7 and T47D breast cancer cells, A549 lung cancer cells, 293 human embryonic kidney cells. **S2C.** Clonogenic survival assay showing the number of colonies in HR-deficient BAP1-mutant MPM cell lines upon transfection with miR223-3p. **S2D.** qRT-PCR showing the levels of miR223-3p in MCF7 cells following BRCA1 knock-down (KD). (**- $p < 0.01$, ***- $p < 0.001$, ****- $p < 0.0001$).

Fig S3A.

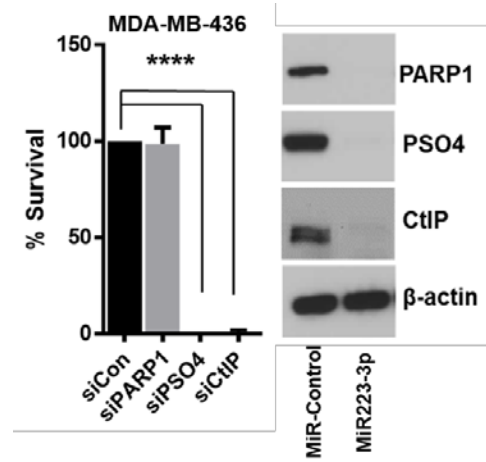


Fig S3B.

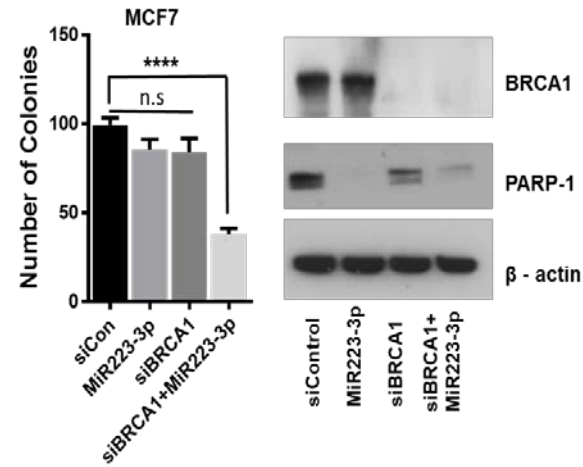
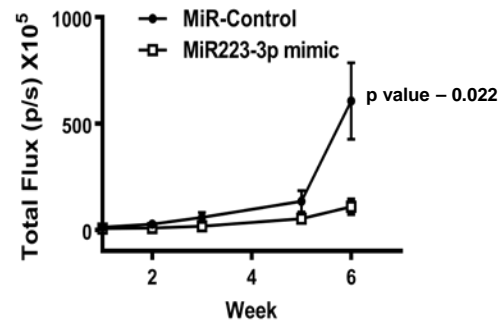


Fig S3C.



Supplementary Figure 3. S3A. Colony formation assay showing percentage survival in MDA-MB-436 cells, and western blot following depletion of PARP1, PSO4 and CtIP. **S3B.** Colony formation assay and western blot in MDA-MB-436 cells following depletion of BRCA1 and PARP1. **S3C.** Graph showing luminescence intensity of tumor (6 weeks) in NSG mice following subcutaneous injection of MDA-MB-436 luciferase cells transfected with either miR-Control or MiR223-3p.

Fig S4A.

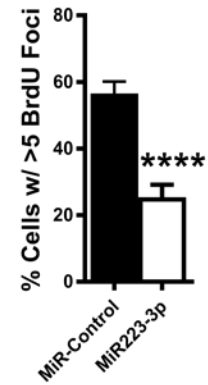


Fig S4B.

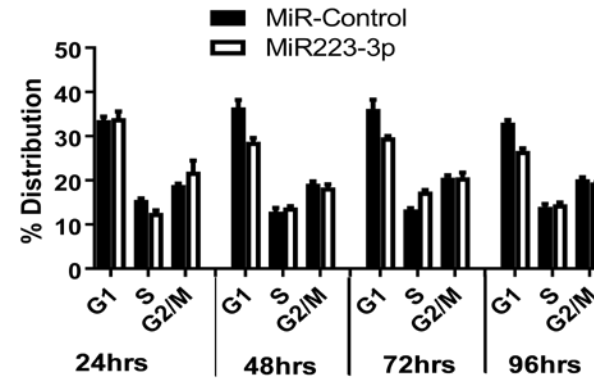
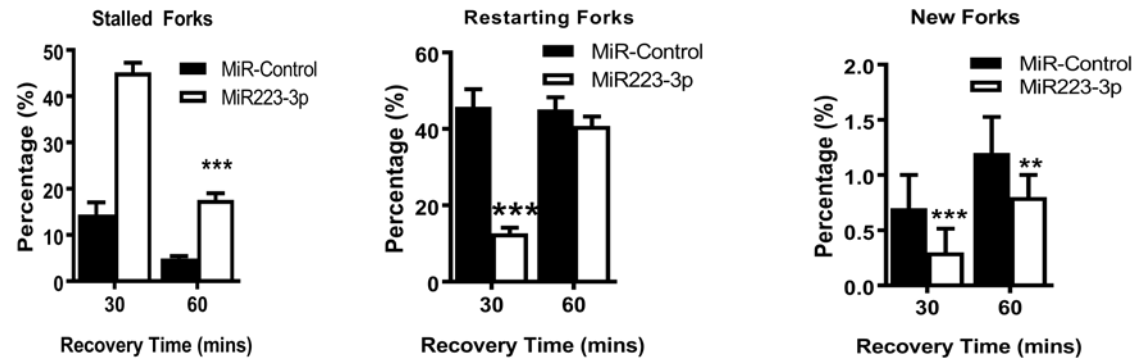


Fig S4C.



Supplementary Figure 4. S4A. Fraction of BrdU-positive cells in control and miR223-3p reconstituted H2452 cells. **S4B.** Cell cycle analysis showing percentage distribution of cells in G1, S and G2/M phases in MDA-MB-436 cells at 24, 48, 72, and 96 hours after miR223-3p transfection. **S4C.** Analysis of stalled forks, restarting forks and initiation of new replication forks in HR-deficient H2452 cells by DNA fiber analysis. (**- $p < 0.01$, ***- $p < 0.001$, ****- $p < 0.0001$).

Fig S5A.

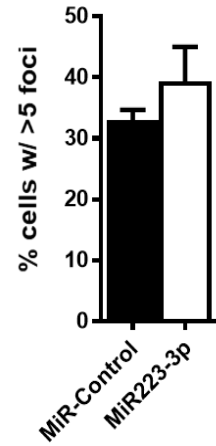
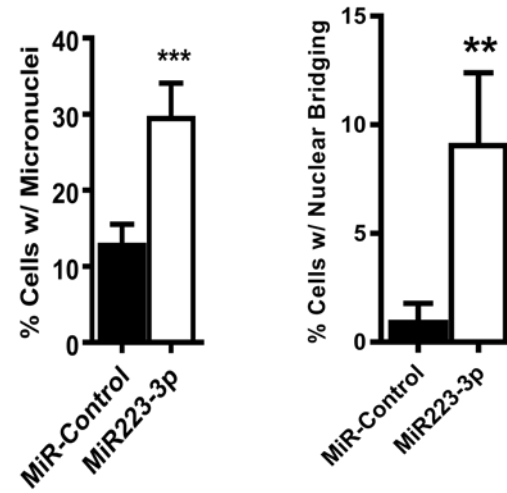


Fig S5B.



Supplementary Figure 5. S5A. Analysis of percentage of cells >5 γ -H2Ax foci in control and miR223-3p reconstituted BAP1-deficient H2452 mesothelioma cells. **S5B.** Analysis of percentage of cells with micronuclei and bridging in H2452 mesothelioma cells. (**- $p < 0.01$, ***- $p < 0.001$).

Supplemental Materials: Antibodies

Rabbit monoclonal PARP1 (Cat # 46D11) antibody used for western blot analysis was purchased from Cell Signaling (Cat# 9532S). Anti-phospho histone H2AX (mouse monoclonal γ -H2AX - S139) was purchased from Millipore (Cat # 05-636), anti-phospho RPA32(S4/S8) was from Bethyl Laboratories (Cat # IHC-00422), and anti-BrdU (Bu20a) was from Cell Signaling (Cat # 5292S). The mouse anti-BrdU antibody and rat anti-BrdU antibody used for DNA fiber analysis were from BD Biosciences (Cat # 347580) and Accurate Chemical (Cat # YSRTMCA2060F), respectively. Ligase III (Cat # sc-56089) and BRCA1 (D-9) (Cat # sc-6954) were purchased from Santa Cruz Biotechnology. DNA polymerase theta antibody was purchased from Novus Biologicals (Cat # H00010721-M09). XRCC1 was purchased from Cell Signaling Technologies (Cat # 2735S). Antibodies used to detect phosphorylated proteins in western blot analyses were: phospho-ATR (p-Thr 1989) antibody purchased from GeneTex (Cat # GTX128145), phospho-ATM (p-Ser1981) (D6H9) from Cell Signaling (Cat # 5883S), phospho RPA32 (S4/S8) antibody from Bethyl Laboratories (Cat # A300-245A), anti-gamma H2Ax from Abcam (Cat # ab11174), phospho-Chk1 (p-Ser317) (D7H2) monoclonal antibody from Cell Signaling (Cat # 8191S), phospho-Chk2 (p-Thr68) from Cell Signaling (Cat # 2661). Other antibodies such as ATR (Cat # 2790S), ATM (D2E2) (Cat # 2873S), Chk1 (2360S), and Chk2 (2662) were purchased from Cell Signaling. The RPA32 antibody was purchased from Bethyl Laboratories (Cat # A300-244A). Alexa Fluor goat anti-mouse 488 conjugate (Cat # A11001) and Alexa Fluor goat anti-rabbit 568 conjugate (Cat # A11011) used for immunofluorescence were purchased from Life Technologies.