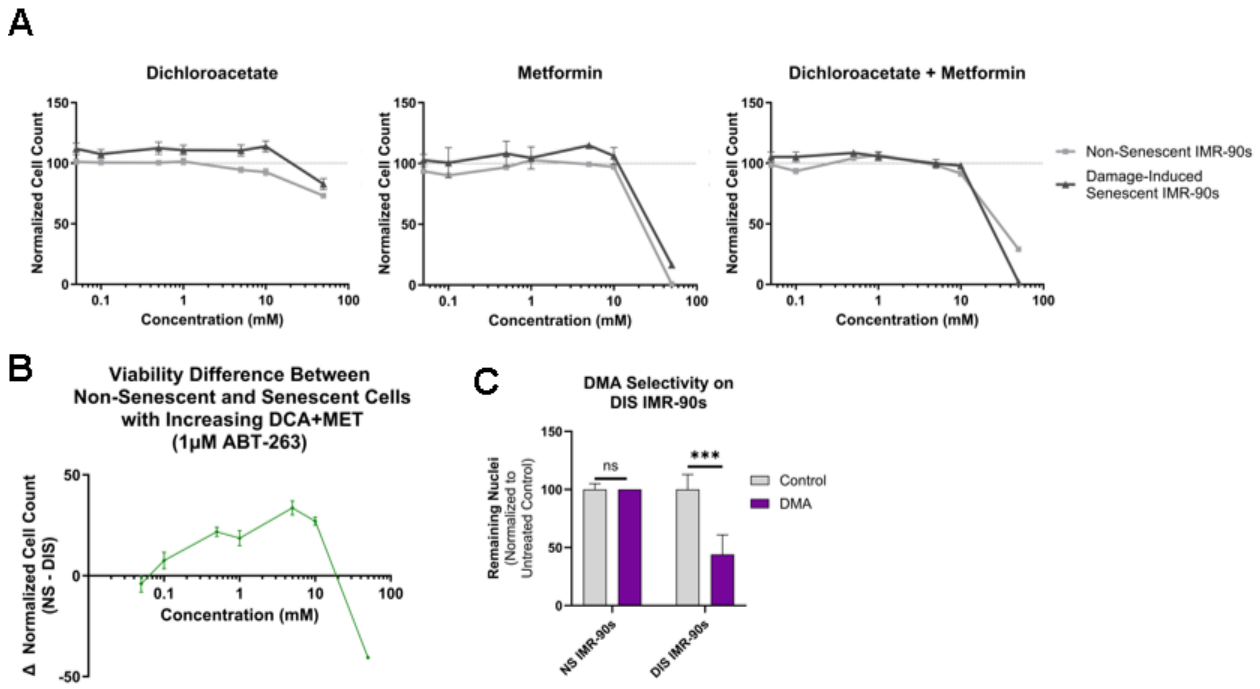
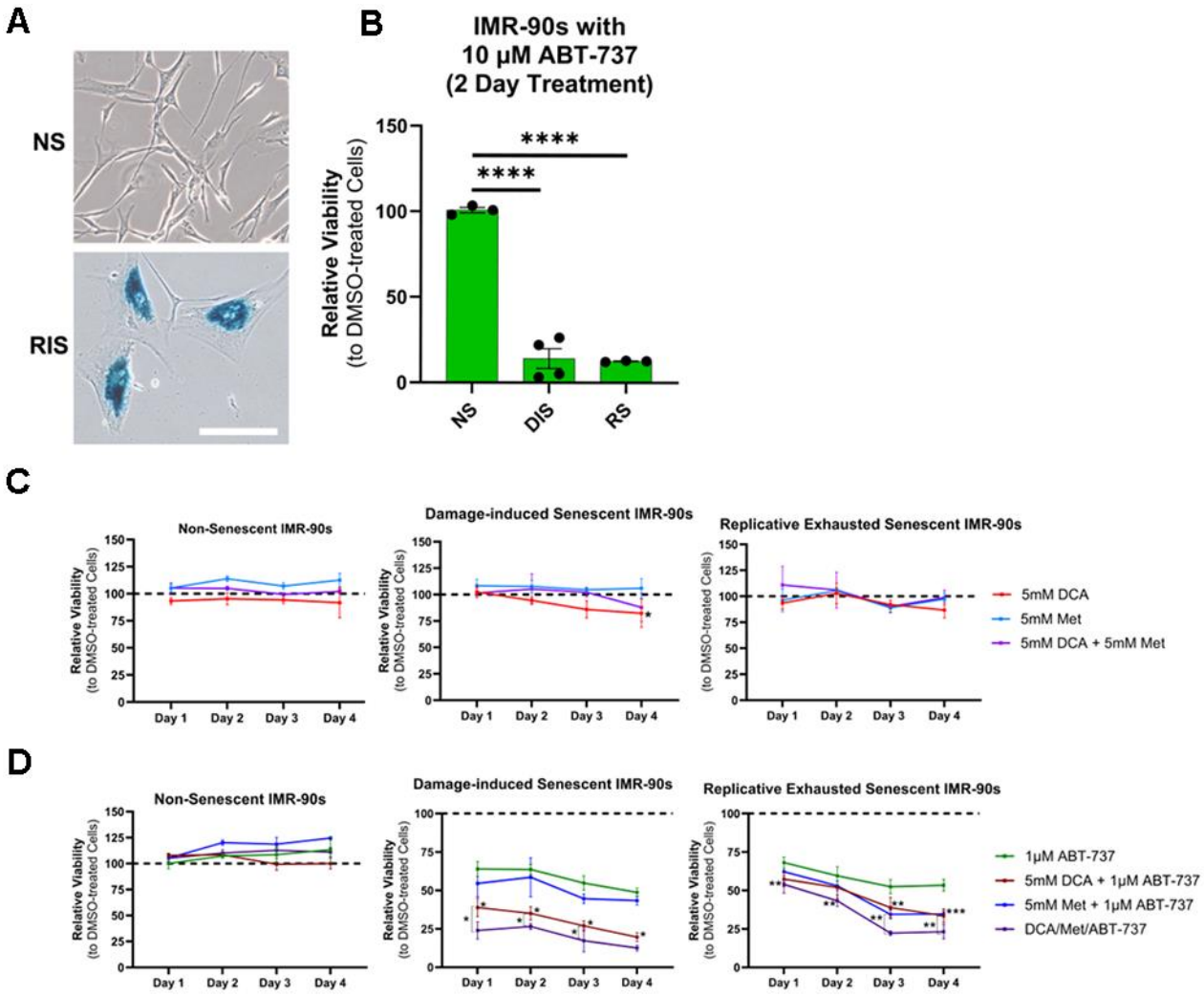
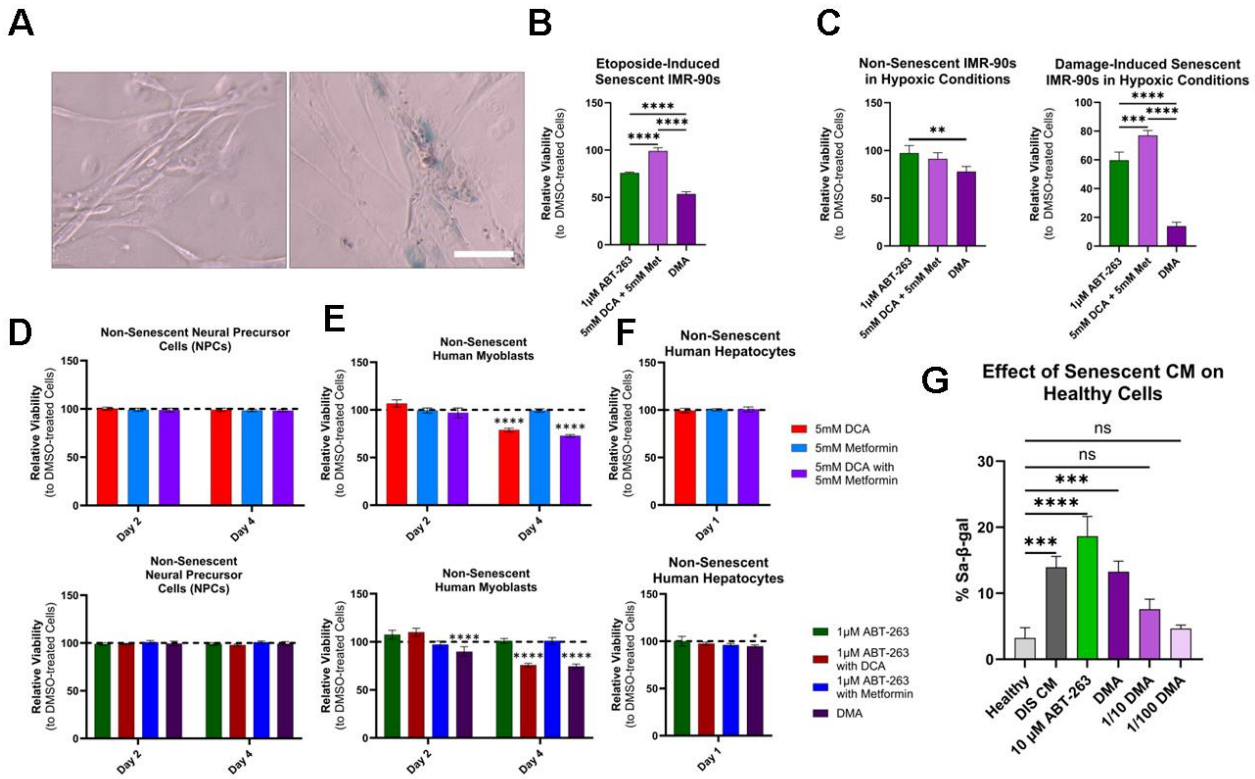
SUPPLEMENTARY FIGURES



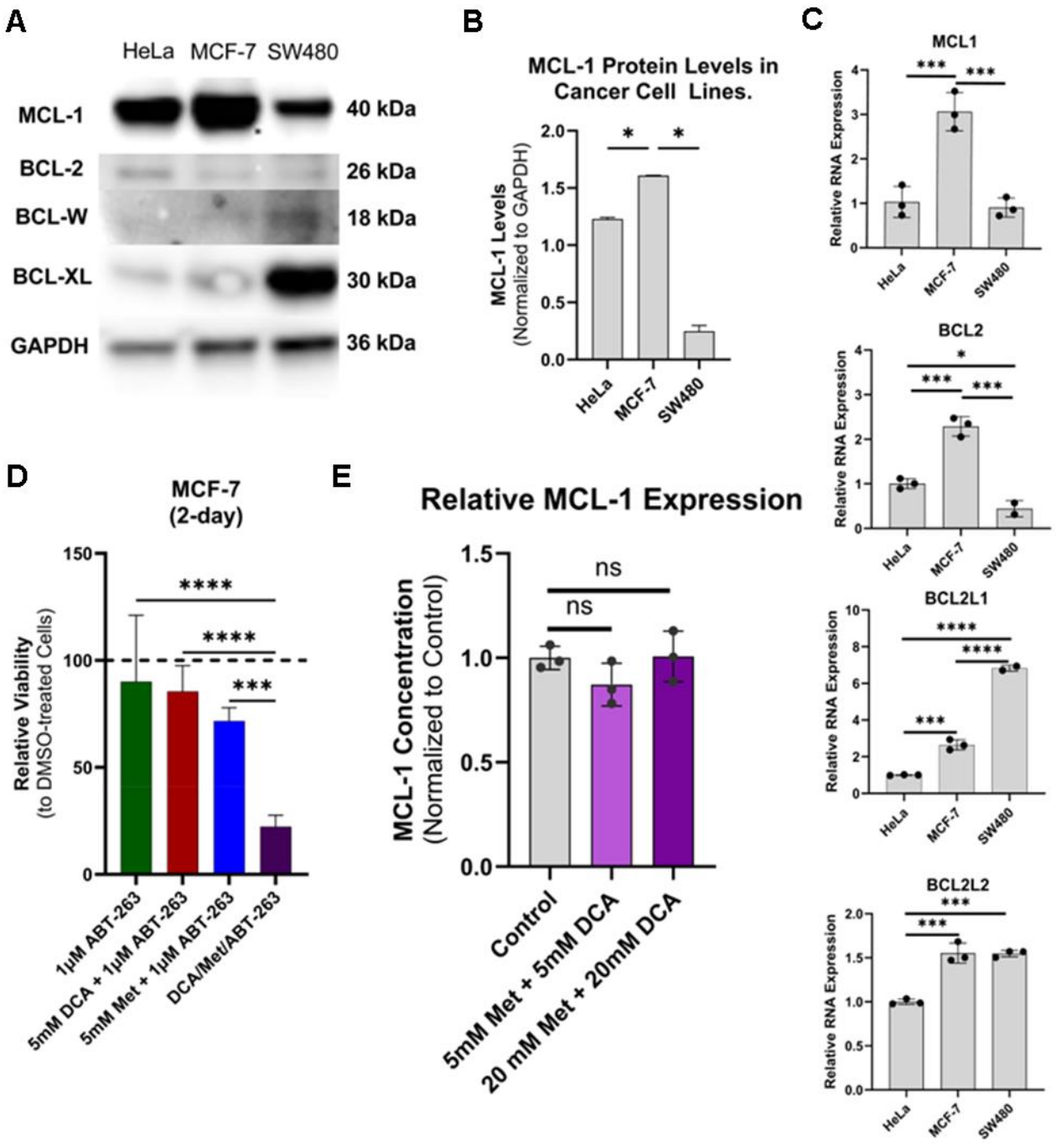
Supplementary Figure 1. Development of DMA. (**A**) Dose curve of DCA and Met alone and in combination on non-senescent (NS) and damage-induced senescence (DIS) IMR-90 cells, as determined by normalized cell count (mean ± SEM). (**B**) Difference in the normalized cell count between NS and DIS cells with increasing concentrations of DCA + Met, with 1μM ABT-263 (mean ± SEM). (**C**) Analysis of remaining nuclei from 3D-Drug Curve with DMA vs control of both NS and DIS IMR-90 cells. (Statistical significance is denoted as: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001).



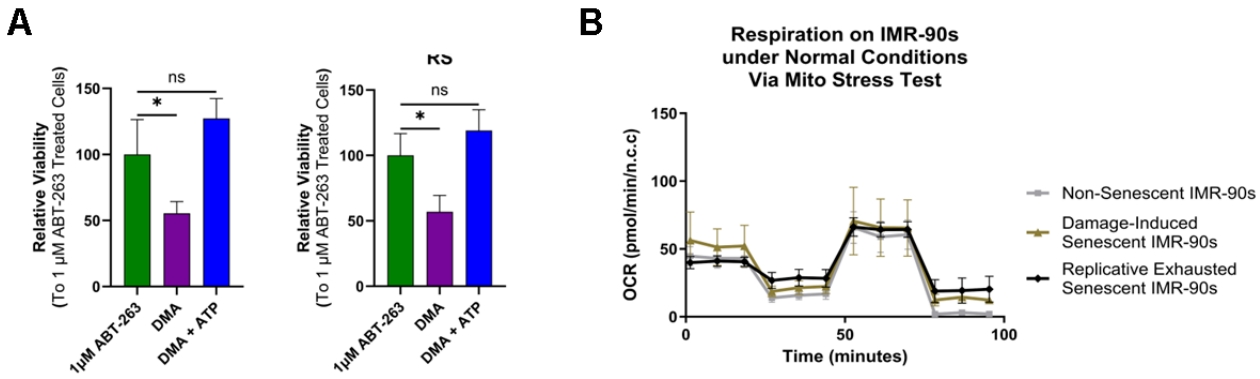
Supplementary Figure 2. Effects of ABT-737 on senescent cells. (**A**) Image of Sa-β-gal of non-senescent (NS) and replicative senescent (RS) IMR-90 cells to confirm senescence (scale bar 200μm). (**B**) Relative viability of IMR-90s on published concentrations of ABT-737 [22], with significantly more viability in NS IMR-90s than DIS or RS (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**C**) Relative viability of NS, DIS, and RS IMR-90 cells treated for 4 days with 5 mM DCA, 5 mM metformin (Met), or both compared to solvent control (dotted line), (mean ± SD, two-way ANOVA, Holm-Šídák test). (**D**) Relative viability of NS, DIS, and RS IMR-90 cells after 4 days of treatment with 1 μM ABT-737 alone or in combination with 5 mM DCA, 5 mM metformin, or both, compared to solvent control (dotted line), (mean ± SD, two-way ANOVA, Holm-Šídák test). (Statistical significance is denoted as: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$).



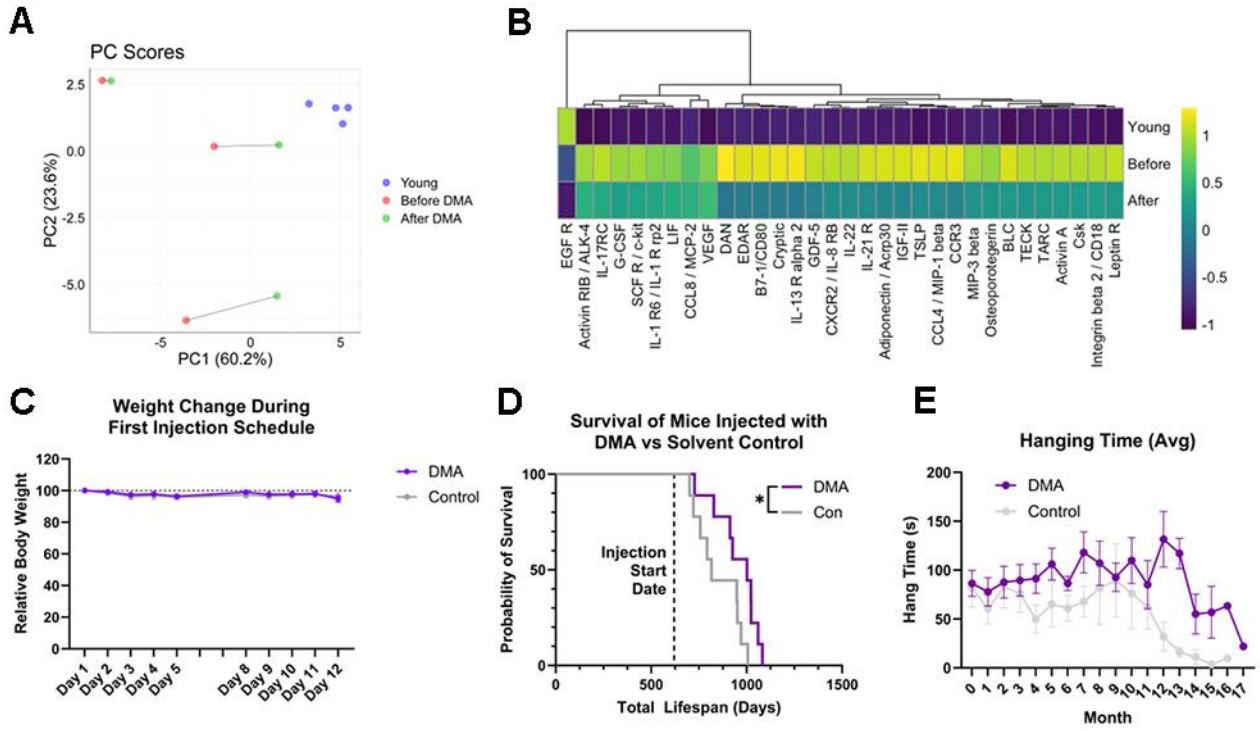
Supplementary Figure 3. Confirming the effects of DMA in different cell types and under different culture conditions. (**A**) SA-β-gal assay confirming etoposide-induced senescence (EIS) compared with NS cells (scale bar 100 μm). (**B**) Relative viability of EIS cells with either 1 μM ABT-263, DCA + Met, or DMA, showing DMA can significantly reduce viability as compared to either condition (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**C**) Treatment of DIS and NS cells in hypoxic conditions with either 1 μM ABT-263, DCA + Met, or DMA showing DIS cells treated with DMA have lower viability than NS cells (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**D**) Relative viability on human NPCs and (**E**) myoblasts with different combinations of 1 μM ABT263, Met, and DCA after 2 and 4 days (mean ± SD, two-way ANOVA, Holm-Šídák test). (**F**) Relative viability of human hepatocytes with different combinations of 1 μM ABT-263, Met, and DCA after 1 day (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**G**) Percent Sa-β-gal-positive recipient cells treated with conditioned media derived from either NS cells or senescent cells cultured with regular media (DIS CM), 10 μM ABT-263, DMA or fold dilutions DMA. Cells treated with cultured media from senescent cells treated with serial dilutions of DMA (1/10 DMA, 1/100 DMA) had no significant difference in the percentage of senescent cells as compared to cells treated with cultured media from NS cells (mean ± SD, two-way ANOVA, Holm-Šídák test). (Statistical significance is denoted as: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$).



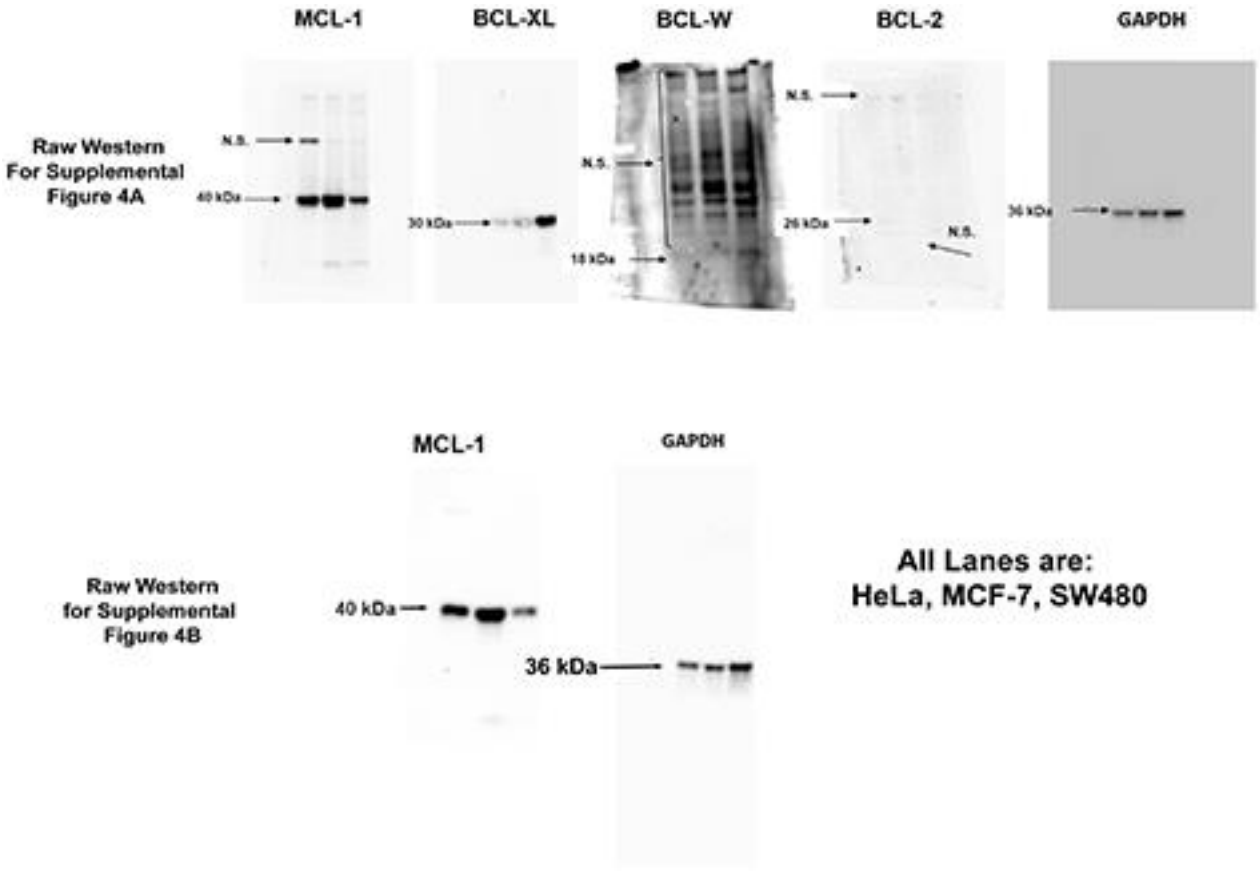
Supplementary Figure 4. Understanding the effects of DMA on cancer cell gene expression. (**A**) Western blot of BCL-2 family proteins of the three cancer cell lines. (**B**) Western blot analysis of MCL-1 levels on three cancer cell lines. MCF-7s have the highest levels of MCL-1 (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**C**) qRT-PCR of BCL-2 proteins from three different human cancer cell lines, normalized by loading control (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**D**) MCF-7s treated with different combinations of 1μM ABT-263 with DCA, Met, or both, showing that the three in combination had the most significant loss of viability compared to either component alone (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**E**) MCL-1 protein levels as determined by ELISA in cells treated with Met and DCA at two concentrations. (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (Statistical significance is denoted as: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$).



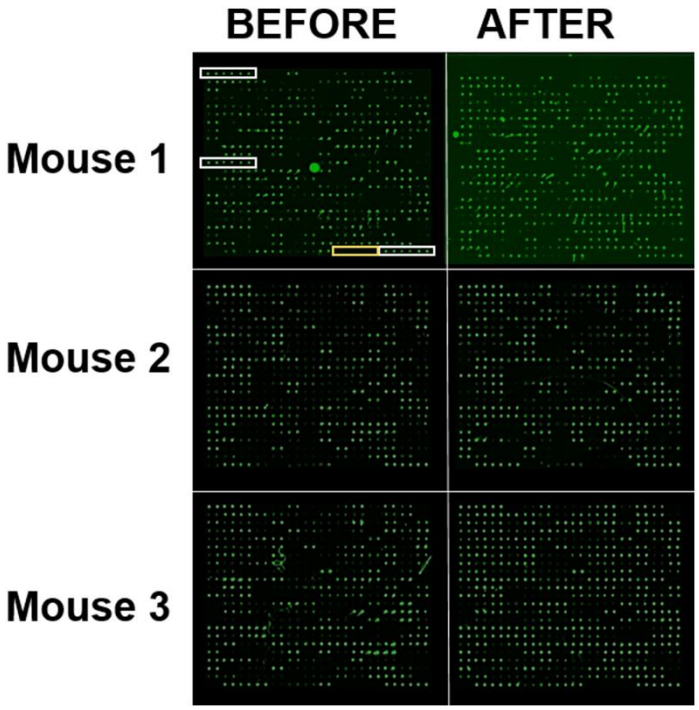
Supplementary Figure 5. Mito-stress test in healthy and SnC, at baseline. (**A**) Effect of exogenous ATP on viability of DIS and RS cells treated with DMA, where exogenous ATP restores viability to levels observed with ABT-263 alone (mean ± SD, one-way ANOVA, Bonferroni's multiple comparisons test). (**B**) Mitochondria stress test on NS, DIS, and RS, normalized by cell count, showing no significant difference between NS and the senescent cell lines (mean ± SD, two-way ANOVA, Holm-Šídák test). (Statistical significance is denoted as: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001).



Supplementary Figure 6. Additional studies on the *in vivo* effects of DMA in old mice. (**A**) PCA plot on comparative proteomics arrays: before vs. after DMA treatment of old mice (with a line connecting matched mice), and untreated young mice. (**B**) Protein expression profiles of young and old mice before and after DMA treatment are shown. Thirty-two proteins that were differentially expressed between young and old mice prior to treatment (Welch's unpaired t-test) are displayed. Expression levels were scaled for each protein, and the mean expression within each group is presented. (**C**) Line graph showing that DMA does not cause a decrease in weight as compared to control (mean ± sem, two-way ANOVA, Holm-Šídák test). (**D**) Survival plot of DMA vs. Control (log-rank (Mantel-Cox) test. n=9,9 Con = 3 male, 6 female, DMA = 5 male, 4 female, median lifespan: Control=815, DMA=1002). (**E**) Longitudinal assessment of hanging endurance in aged mice following DMA treatment (mean± sem, linear mixed-effects model). (Statistical significance is denoted as: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001).



Supplementary Figure 7. Full Western blots used in Supplementary Figure 4A, 4B. Lanes are HeLa, MCF-7, and SW480 for bottom Westerns.



Supplementary Figure 8. The scans of antibody arrays. RayBiotech arrays (Raybiotech, Mouse L308 Array) were scanned on Genepix 4400A scanner at 450 PMT; the built-in positive (white) and negative (yellow) controls are outlined on the top scan.