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Supplemental Data

MGMT Inhibition Restores ERα Functional Sensitivity to Antiestrogen Therapy

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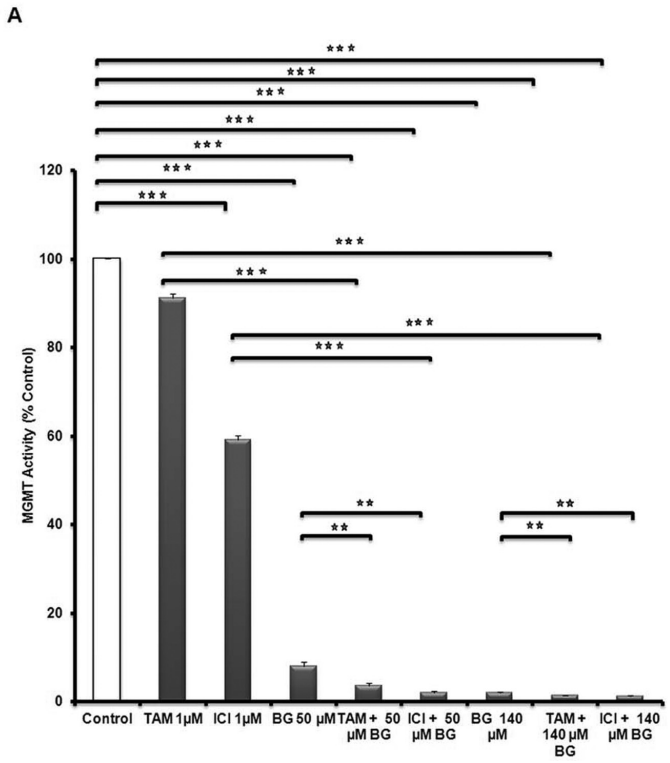

Supplementary Figure S1. Benzylguanine inhibits tamoxifen-resistant breast cancer growth in an MGMT independent manner. Tamoxifen-resistant MCF7 breast cancer cells were treated with BG (50 or 140 μmol/L) for 24 h before TAM/ICI was added for 48 h before MGMT activity assay was performed. (A) BG (50 or 140 μmol/L) led to significant decrease in MGMT activity which was decreased further when combination therapy (TAM + BG/ICI + BG) was used. (B) Tamoxifen-resistant MCF7 cells were transfected with NT siRNA or MGMT siRNA and 24h post transfection BG (50 or 140 μmol/L) was added for another 48 h before ATP assays were performed. BG (50 μmol/L) did not inhibit tamoxifen-resistant MCF7 cell growth whereas BG (140 μmol/L) showed 50% growth inhibition. Addition of BG (140 μmol/L) to MGMT siRNA showed an enhancement of growth inhibition over MGMT siRNA alone. (C) BG (50 μmol/L) did not have any growth inhibitory effect either alone or in combination with TAM/ICI. BG (140 μmol/L) either alone or in combination with TAM/ICI significantly decreased tamoxifen-resistant breast cancer cell growth.

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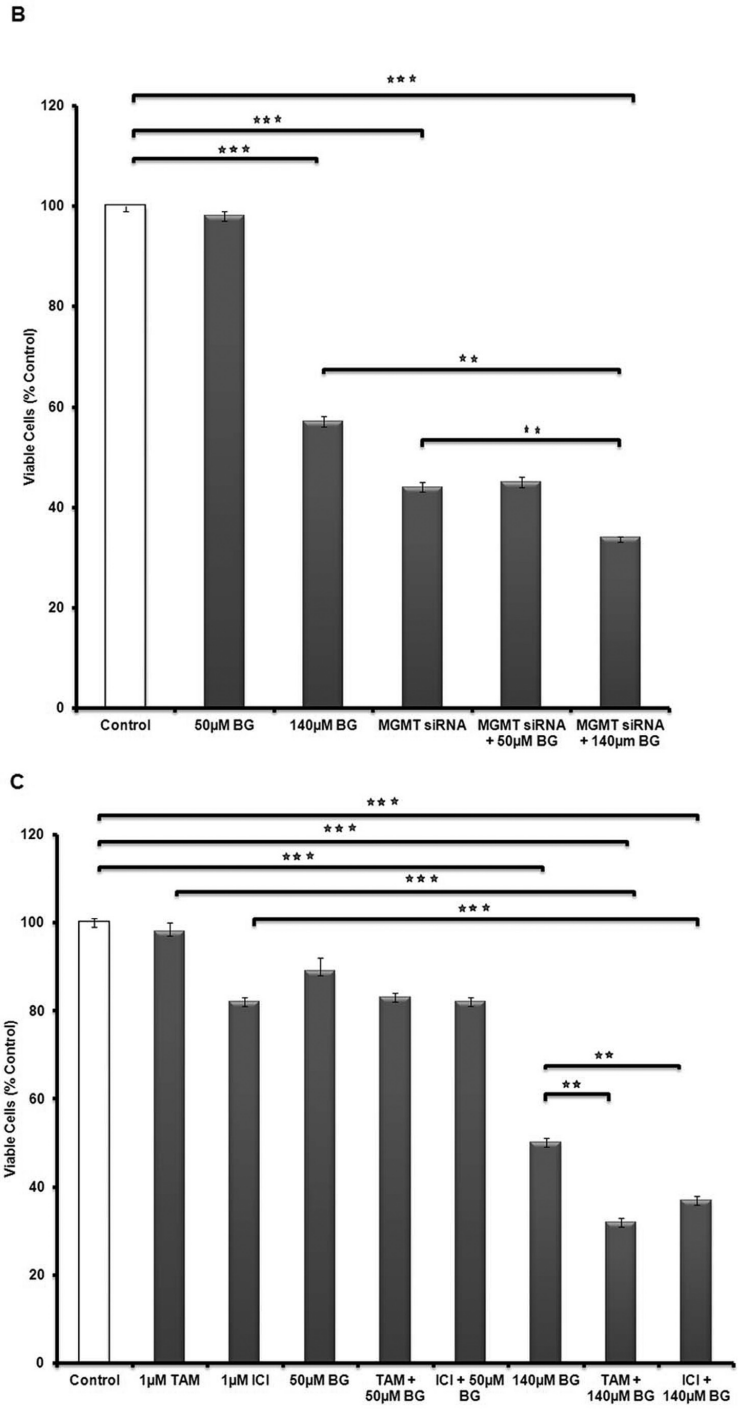
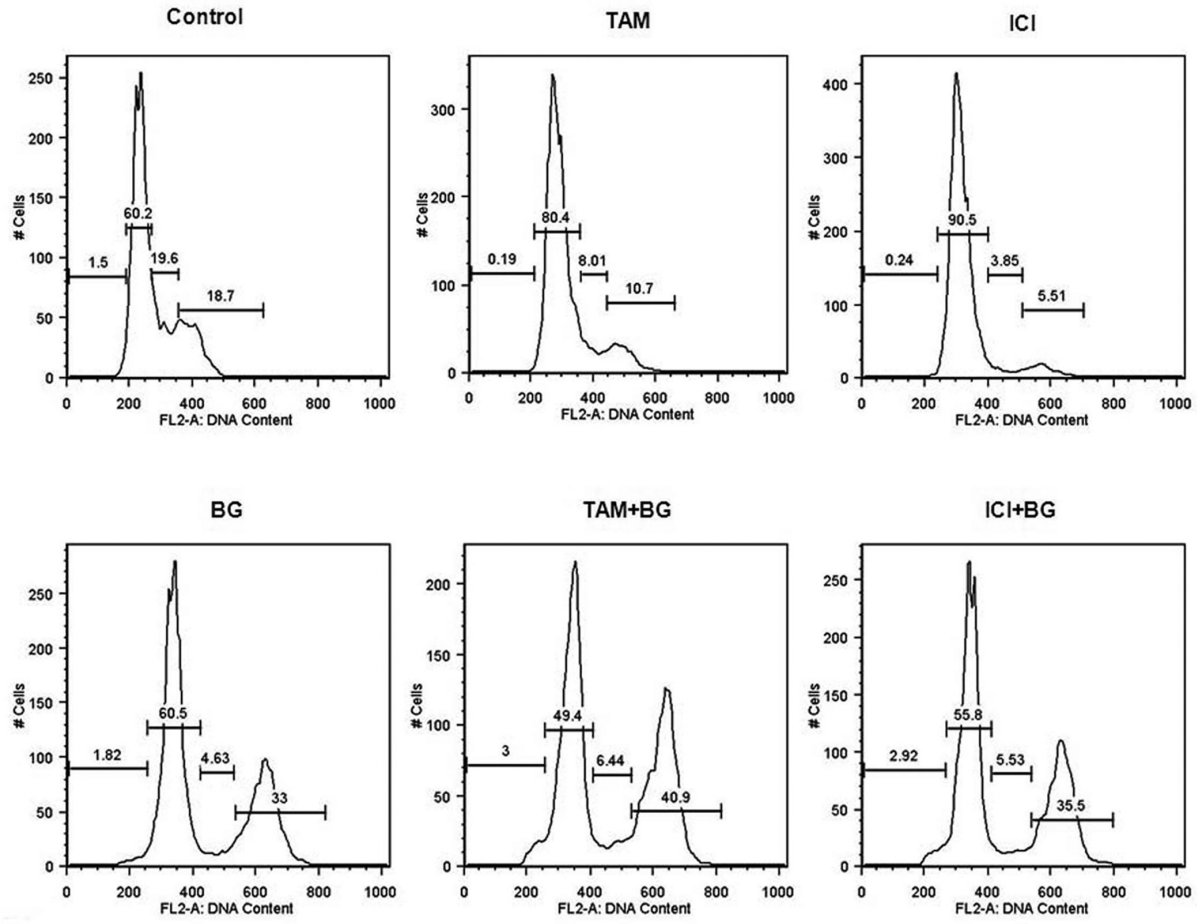


Supplementary Figure S1. *Continued.*



Supplementary Figure S2. Benzylguanine and combination therapy induces G2/M arrest. Tamoxifen-resistant MCF7 breast cancer cells were treated with BG (140 μmol/L) for 24 h before TAM or ICI was added for another 48 h before flow cytometry analysis was performed. BG (140 μmol/L) led to significant G2/M arrest (promoting cytostasis and cell death) which was further enhanced in the presence of combination therapy (TAM + BG/ICI + BG).