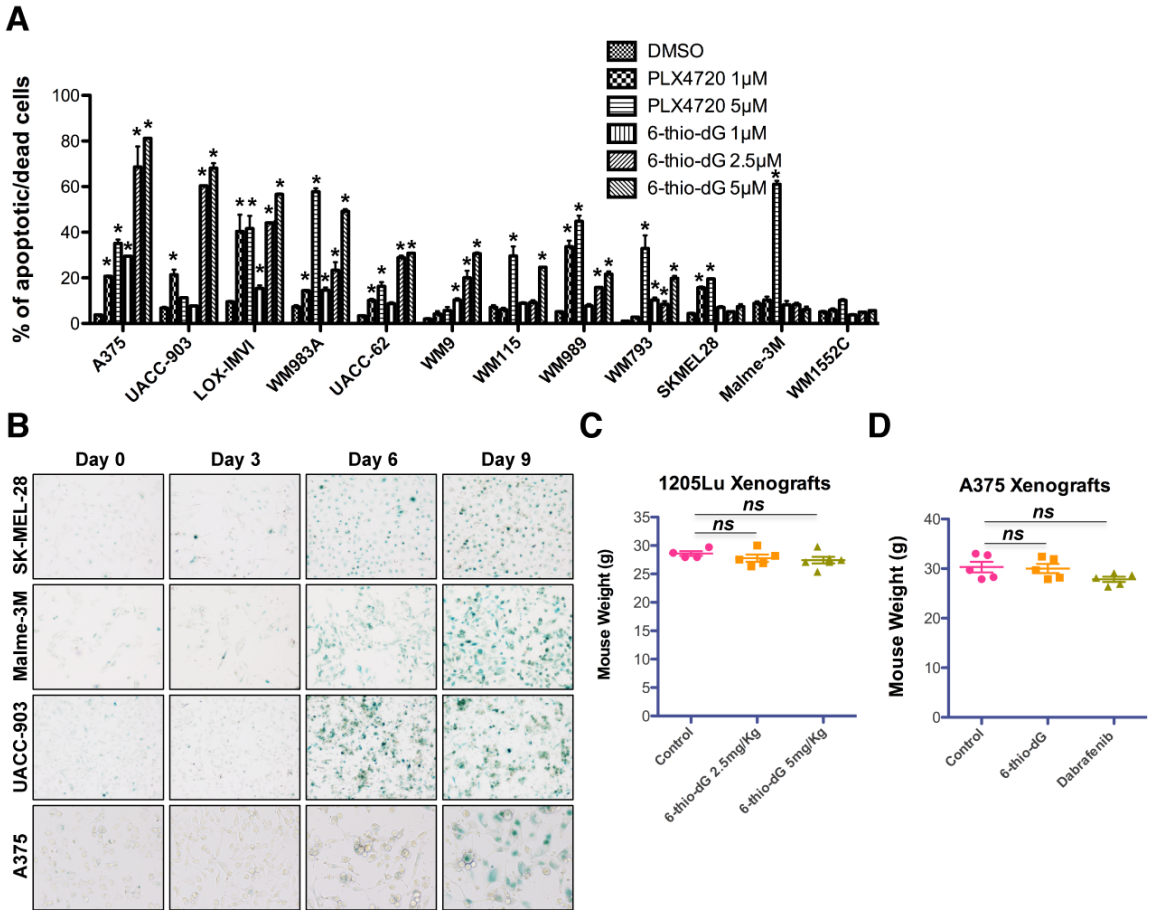
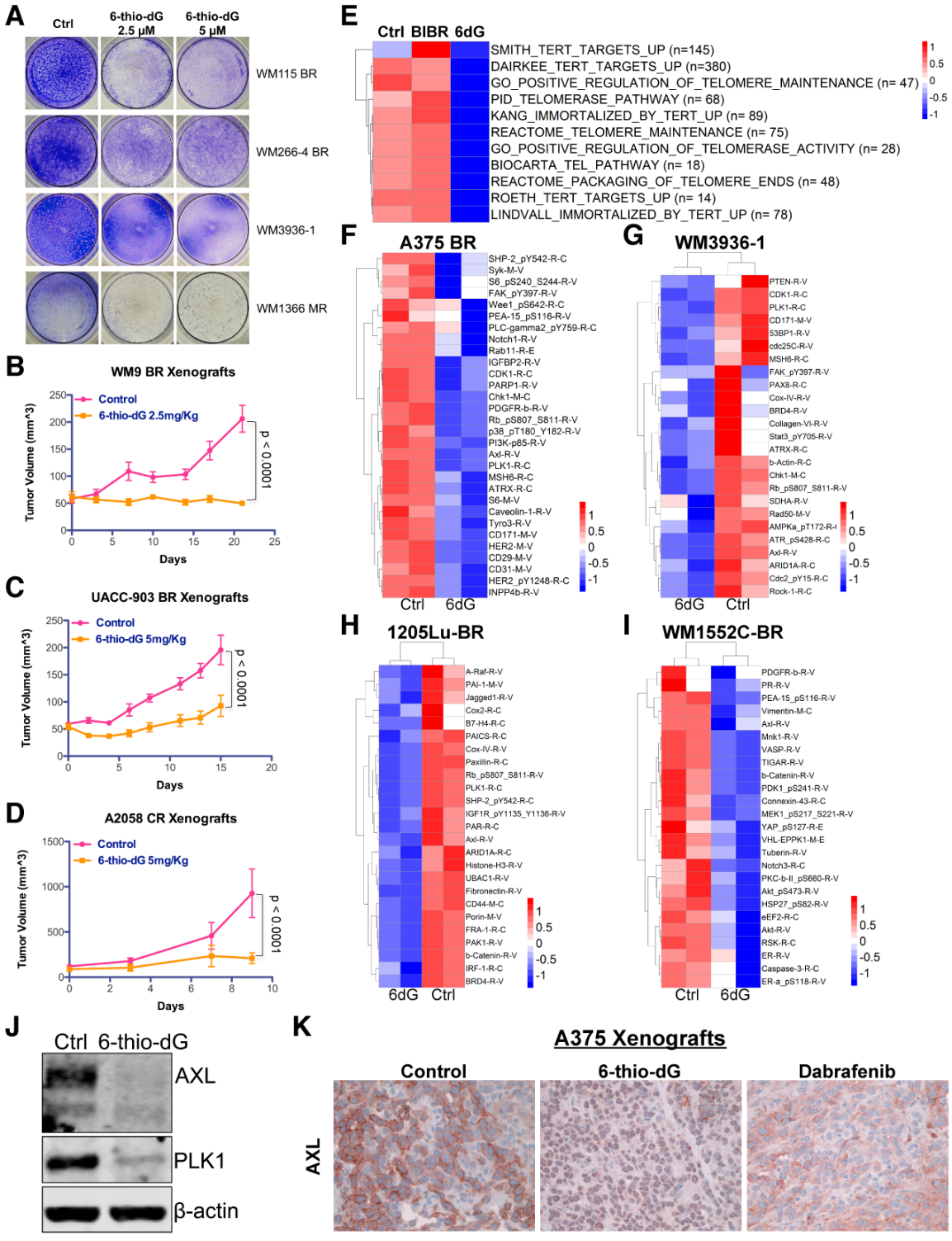
# Supplementary Figures and Tables




**Supplementary Fig. 1: Related to Fig. 2**

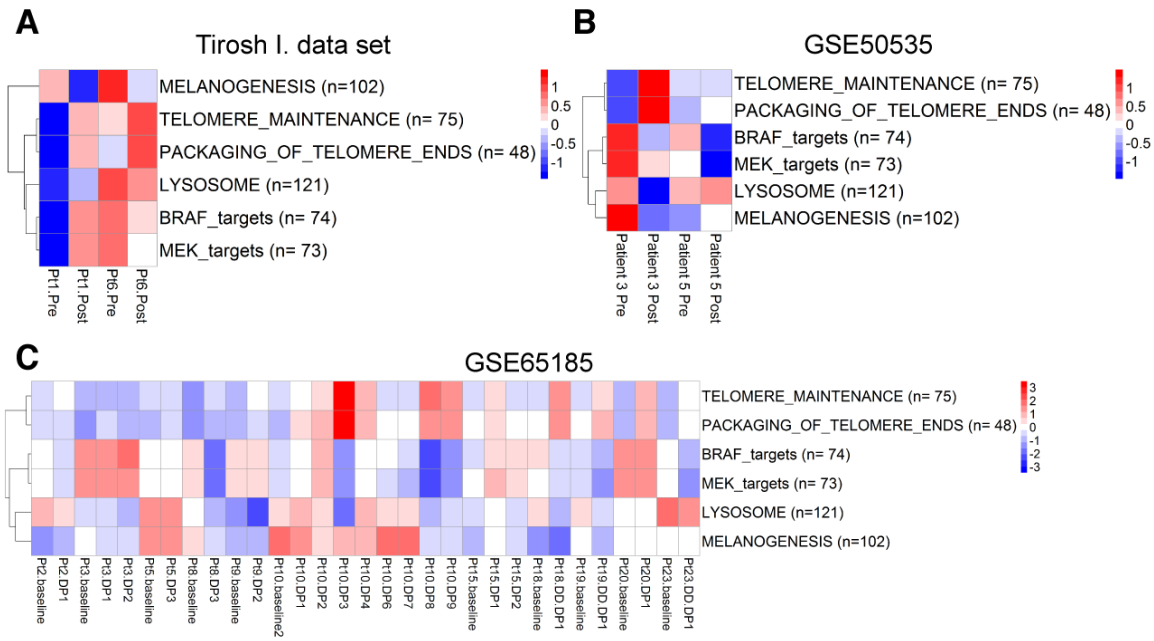
(**A**) The percentage of apoptotic and dead cells indicated as PSVue $643^{+}$ cells in each of 12 *BRAF*-mutant melanoma cell lines treated with PLX4720 or 6-thio-dG at indicated doses for 120 hours. Cells were then harvested and co-stained with PSVue643 and Propidium iodide (PI). The average of 2 biological replicates was plotted. (**B**) SA-β-gal staining of 4 *BRAF*-mutant melanoma cell lines treated with 6-thio-dG at 5μM for 9 days. A representative image of 3 biological replicates was shown for each experimental sample. (**C** and **D**) Mouse weights of 1205Lu (**C**) and A375 (**D**) xenografts in each treatment group were shown.




**Supplementary Fig. 2: Related to Fig. 4**

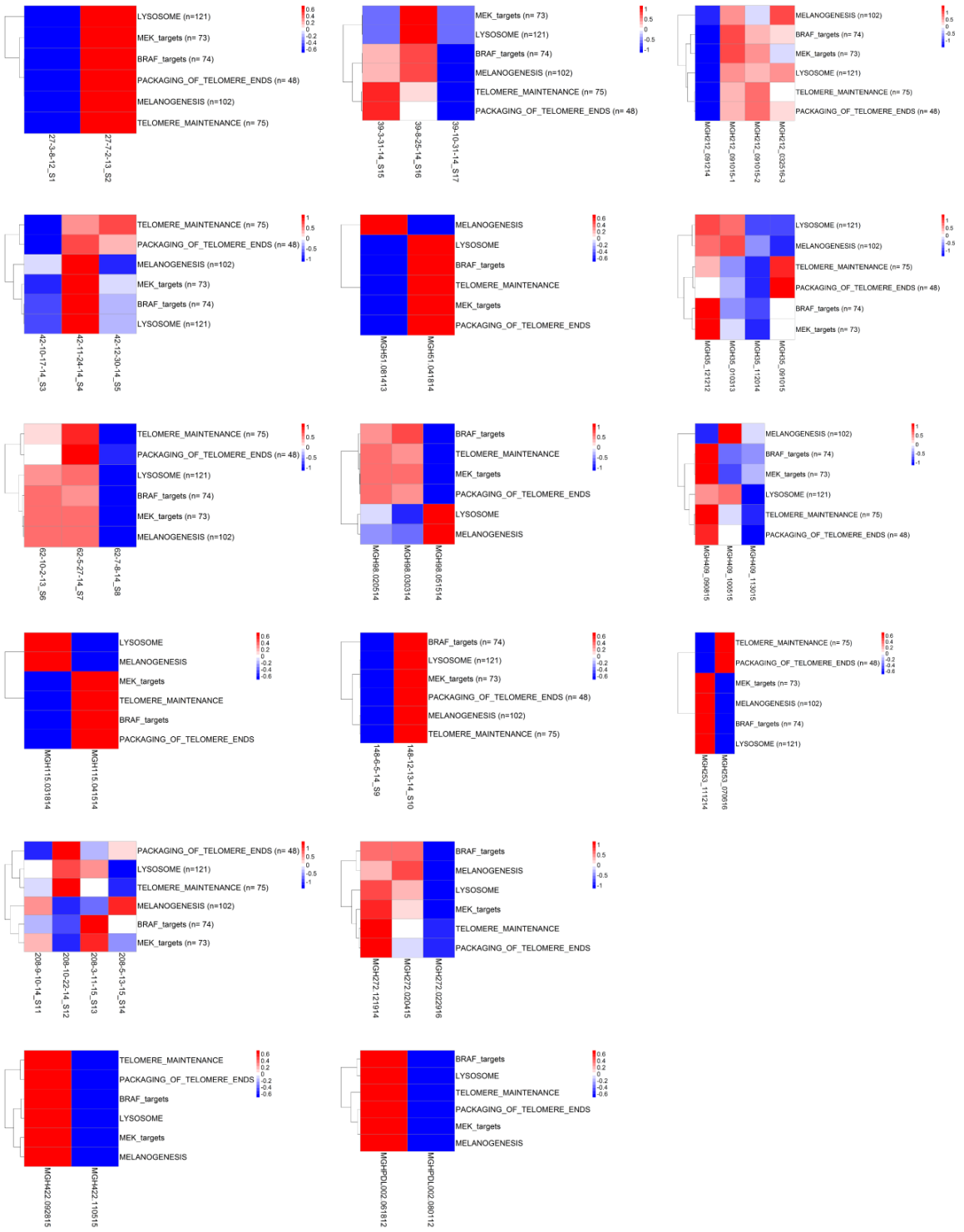
(**A**) Long-term cell growth assay of 4 melanoma cell lines that acquired resistance to MAPKi treated with 6-thio-dG at indicated doses for 12 days. Cells were then fixed and stained with

crystal violet. A representative image of 2 biological replicates was shown for each experimental condition. (**B-D**) Tumor volumes of WM9 BR (**B**), UACC-903 BR (**C**) and A2058 CR (**D**) xenografts that were treated with the vehicle control and 6-thio-dG at indicated doses. (**E**) The ssGSEA plot of 11 MSigDB gene sets related to telomere and telomerase that were significantly altered in LOX-IMVI BR cells treated with BIBR 1532 (BIBR) or 6-thio-dG (6dG). (**F-I**) The heatmaps of RPPA data depicting 30 proteins that were most significantly down-regulated in four representative BR cell lines treated with 6-thio-dG, including A375 BR (**F**), WM3936-1 (**G**), 1205Lu BR (**H**) and WM1552C BR (**I**). (**J**) Western blotting of proteins that were down-regulated in LOX-IMVI BR cells treated with 6-thio-dG (6dG). (**K**) The immnohistochemical analysis of AXL was performed in A375 tumors that were treated with the control, 6-thio-dG and Dabrafenib.



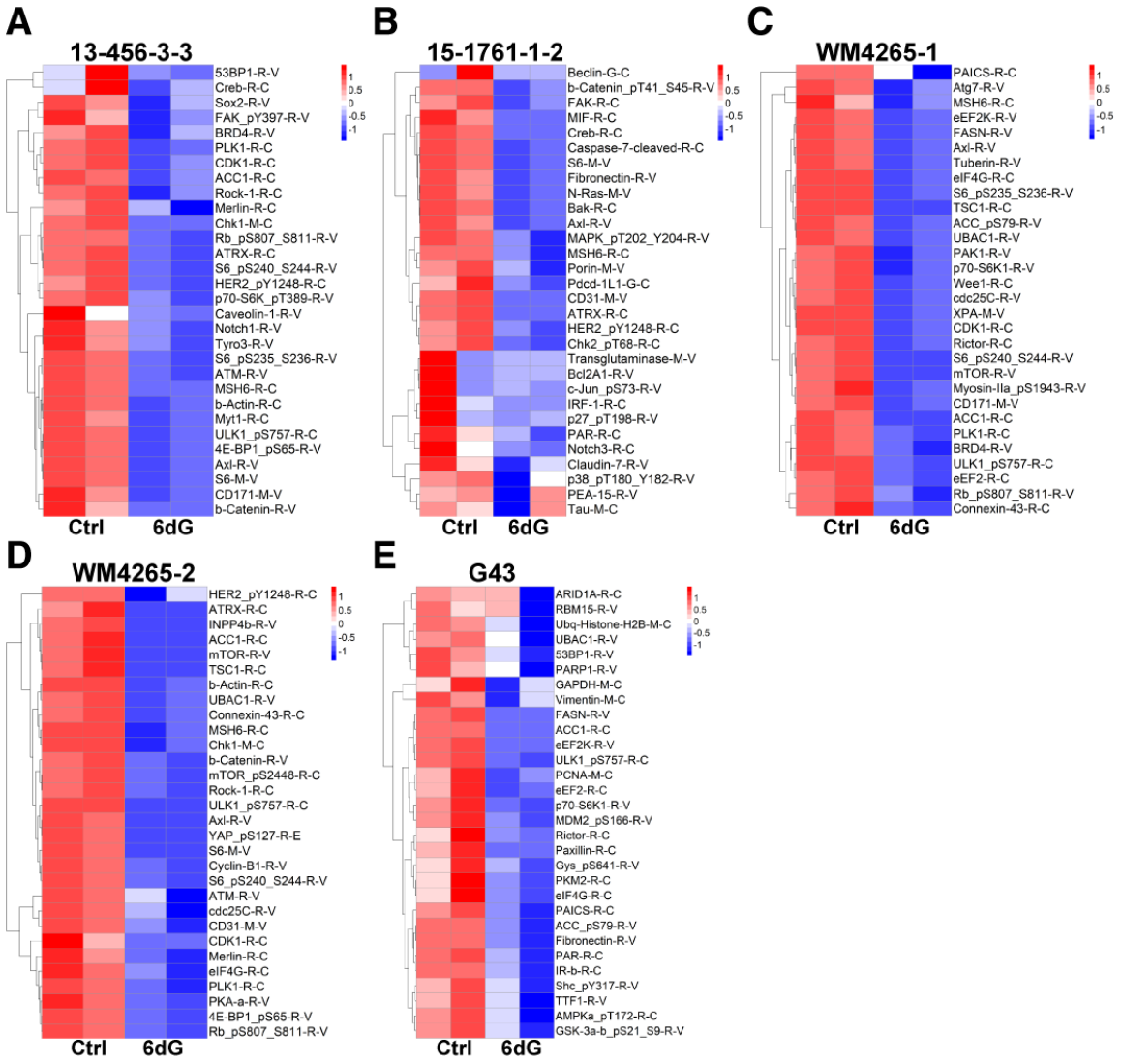

**Supplementary Fig. S3: Related to Fig. 5**

(**A-C**) The heatmaps of two telomere transcriptional gene signatures, two melanoma-specific gene sets and two MAPK pathway-related gene sets in three datasets in which transcriptomes of paired pre- and post-treatment tumor biopsies derived from patients who progressed on MAPKi were profiled.




**Supplementary Fig. S4: Related to Fig. 5**

The heatmaps of two telomere transcriptional gene signatures, two melanoma-specific gene sets and two MAPK pathway-related gene sets in paired pre-, on- and post-treatment tumor biopsies derived from 16 patients who were treated with immunotherapies.




**Supplementary Fig. S5: Related to Fig. 6**

(**A-E**) The heatmaps of RPPA data depicting 30 proteins that were most significantly down-regulated in 5 short-term cultures or cell lines derived from immunotherapy-resistant tumors that were treated with 6-thio-dG, including 13-456-3-3 (**A**), 15-1761-1-2 (**B**), WM4265-1 (**C**), WM4265-2 (**D**) and G43 (**E**).