Supplementary Figure Legends

Supplementary Figure 1. siRNA induces concentration-dependent senescence in PC-3, SNU484, and MKN74 cells, but not in normal prostate epithelial cells (PrEC). Cells were stained for SA-β-Gal 5 days after transfection with the indicated concentrations of siRNAs.

Supplementary Figure 2. TUNEL assay using an *in situ* death detection kit. PC-3 cells transfected with siKir2.2 or siC (30 nM) were harvested on post-transfection day 5, and cell death was estimated. Cells were visualized by fluorescence microscopy. PBS and etoposide (1 μg/ml for 48 hours) were used as negative and positive controls, respectively.

Supplementary Figure 3. Kir2.2 knockdown induces cell-cycle arrest in MKN74 cells. ***A.*** Effect of Kir2.2 knockdown on the cell-cycle distribution. Cells transfected with the indicated siRNA were collected 48 hours after transfection and subjected to a flow cytometric analysis. The values shown represent the mean ± SD (bars) of three independent experiments. ***B.*** Changes in the expression of cell cycle-related proteins following siRNA transfection. Cells harvested at the indicated intervals were lysed, and cell lysates containing 20 μg of protein were analyzed by SDS-PAGE/Western blotting using the antibodies shown on the right.

Supplementary Figure 4. Kir2.2-specific modulation of cancer cell senescence. ***A.*** Specificity of siRNA for the knockdown of each Kir2.x. PC-3 cells transfected with the indicated siRNA (50 nM) were harvested and evaluated for the expression of each Kir2.x isoform by RT-PCR. Primers used to generate cDNAs are listed in Supplementary Figure 4. ***B.*** Knockdown of Kir2.2, but not other Kir2.x isoforms, induced senescence in PC-3. The number on the bottom indicates the percentage of SA-β-Gal-positive cells.

Supplementary Figure 5. siKir2.2 induces irreversible senescence in multiple cancer cells. ***A.*** Prostate cancer cells (PC-3, DU145, and LNCaP), stomach cancer cells (MKN74 and SNU668), and breast cancer cells (MCF7, SK-BR-3, and T47D) were stained for SA-β-Gal 5 days after transfection with siRNAs. ***B.*** Long-term growth and phenotypic changes in PC-3 cells after knockdown of Kir2.2. PC-3 cells were stained for SA-β-Gal at the indicated times after siRNA transfection.

Supplementary Figure 6. Kir2.2-modulated PC-3 cell growth is independent of potassium concentration or channel function. ***A.*** Incubation with the potassium channel blocker $BaCl_2$ (0.5 mM) did not affect cell growth. ***B.*** The addition of KCl (15 mM) to the culture medium did not

prevent doxorubicin-induced cell growth inhibition.