cancers

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Article - Supplementary Images

Microtubule Dynamics Deregulation Induces Apoptosis in Human Urothelial Bladder Cancer Cells via a p53-independent Pathway

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Supplementary Images

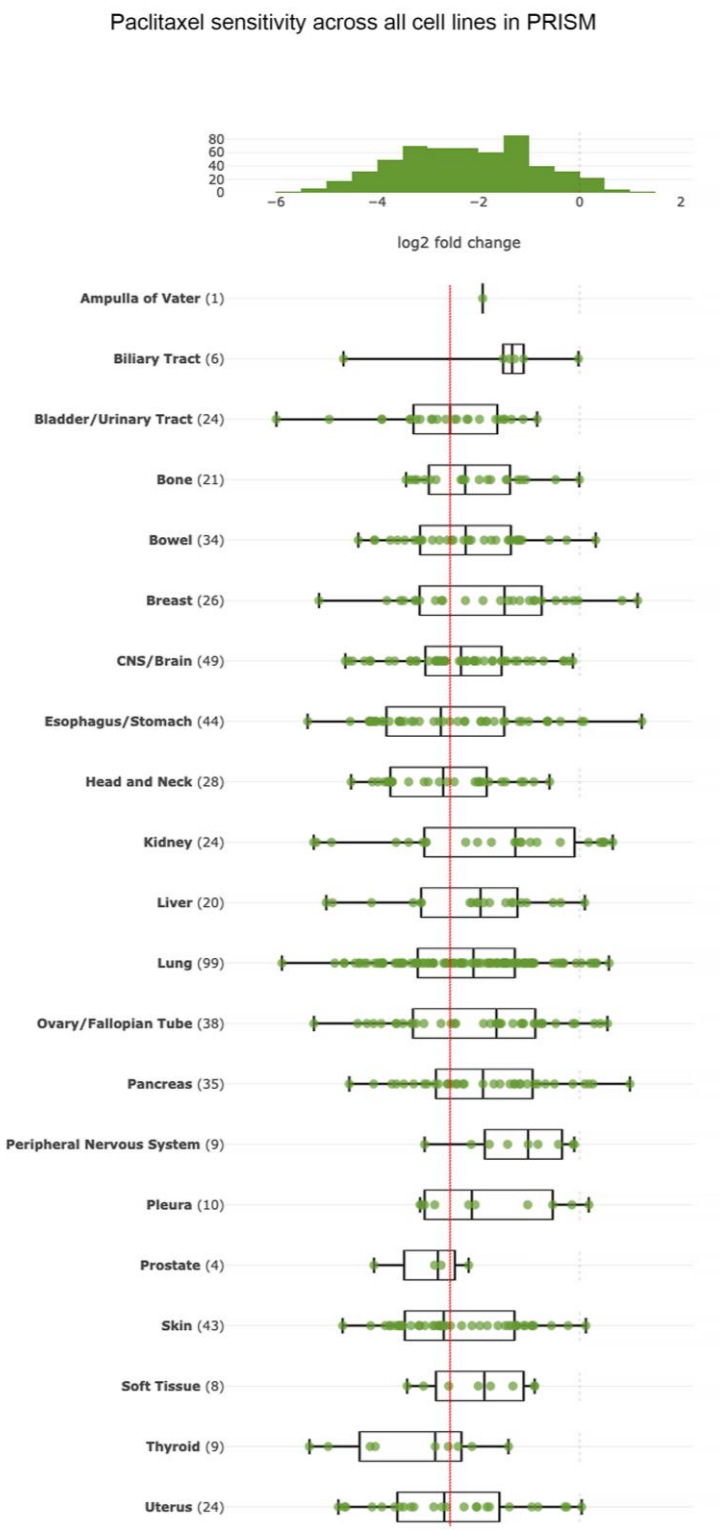

Figure S1. BLCA cell lines are among the most sensitive to paclitaxel treatment. Viability analysis as measured by the log2 fold change of barcoded cells at day 5 compared to day 0 (see text for details) of Paclitaxel treatment. In total, 499 cell lines from 21 lineages/cancer types were analyzed and the log2 fold changes for each lineage are plotted as box plots. The median log2 fold change in viability for BLCA cells (-2.55) was lower compared to lung (-2.1), breast (-1.56) or ovarian carcinoma (-1.65) where Paclitaxel is a standard of care treatment.

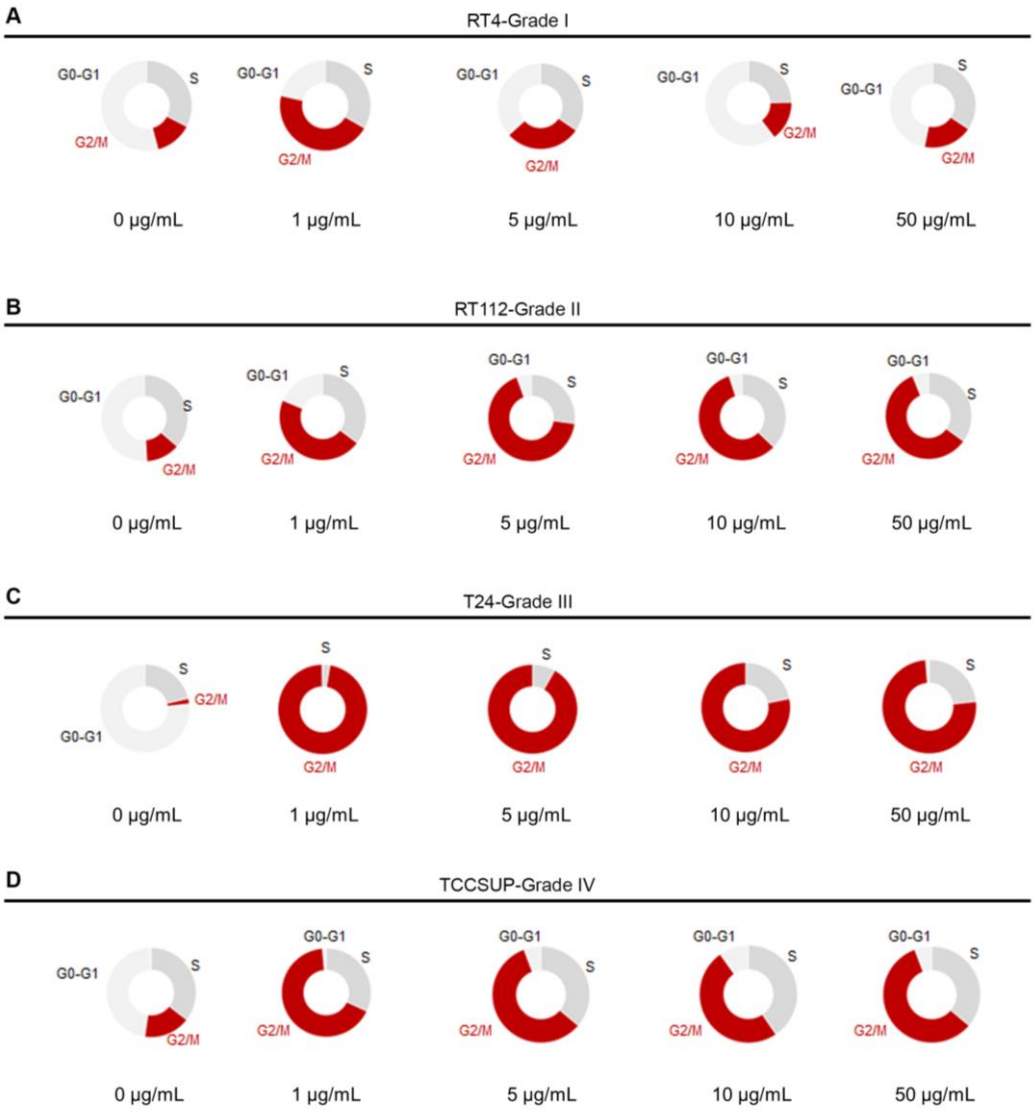

Figure S2. Paclitaxel treatment induces cell cycle arrest in BLCA cell lines. (A) Flow cytometry analysis of RT4 cells either untreated (0 µg/mL) or treated with a dose range of Paclitaxel (1-50 µg/mL). (B) Flow cytometry analysis of RT112 cells either untreated (0 µg/mL) or treated with a dose range of Paclitaxel (1-50 µg/mL). (C) Flow cytometry analysis of T24 cells either untreated (0 µg/mL) or treated with a dose range of Paclitaxel (1-50 µg/mL). (D) Flow cytometry analysis of TCCSUP cells either untreated (0 µg/mL) or treated with a dose range of Paclitaxel (1-50 µg/mL).

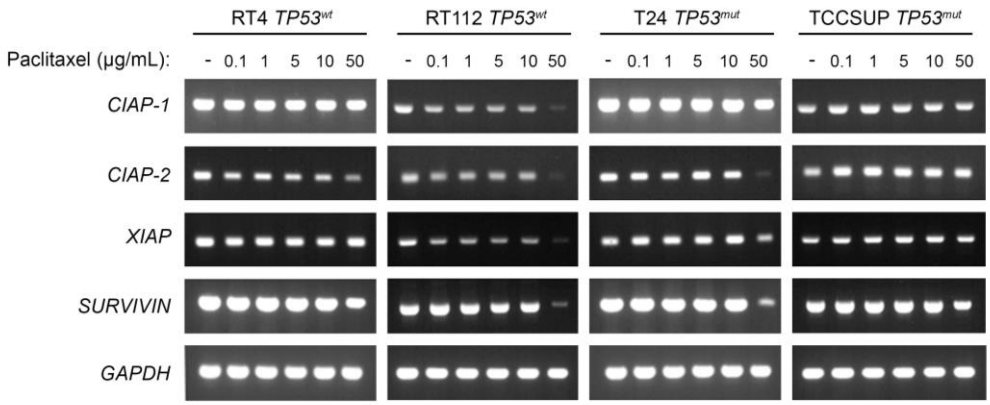

Figure S3. BLCA cell lines express high levels of pro-apoptotic genes. RT-sqPCR analysis of total RNA extracted from RT4, RT112, T24 and TCCSUP cells, seeded at ~60 % confluency and exposed to the indicated doses of Paclitaxel for 24 h. Expression of *CIAP-1*, *CIAP-2*, *XIAP* and *SURVIVIN* indicate that BLCA cells have a fully functional pro-apoptotic machinery.

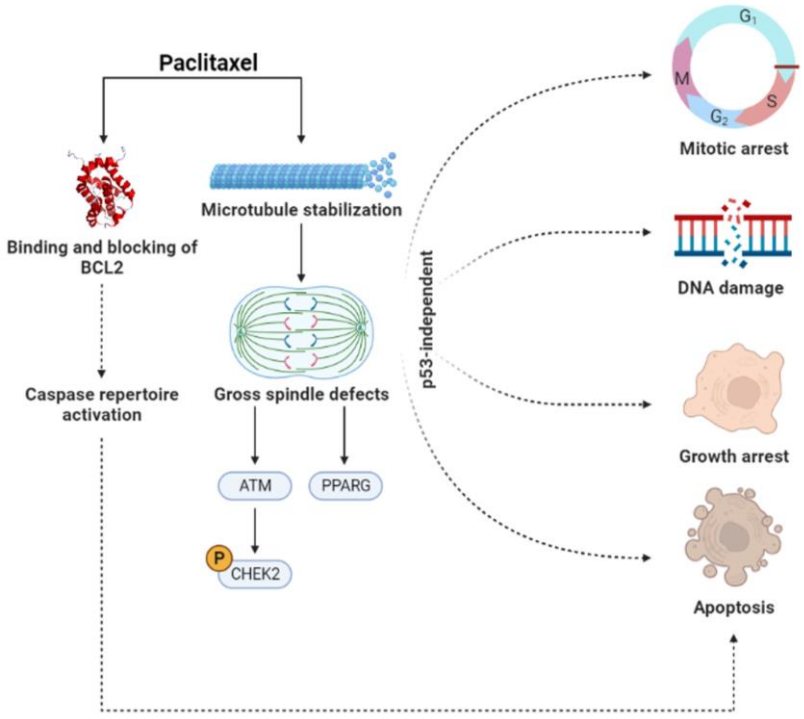

Figure S4. Mechanistic model. Paclitaxel treatment blocks microtubule depolymerization and induces an ATM-dependent but p53-independent DNA damage response, which results in G2-M cell cycle arrest, growth arrest and apoptosis. In parallel, paclitaxel can directly bind to BCL2 and block its anti-apoptotic activity, further inducing caspase-mediated apoptosis.