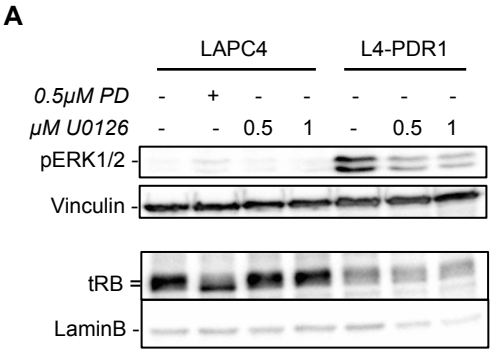

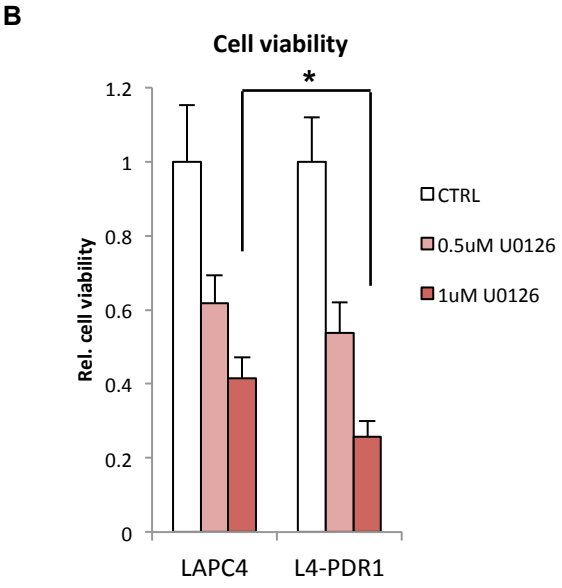

Supplementary Figure 6: Acquired CDK4/6i resistance leads to dependence on MAPK signaling. A. LAPC4 cells were treated 24h with 0.5 or 1μM MEK inhibitor (U0126) or CTRL and immunoblotted for p-ERK1/2, demonstrating loss of the hyperphosphorylation of ERK1/2 observed in the LNCaP PDR models when MEK is inhibited, confirming that the MAPK pathway is activated in the PDR models. MEK inhibition does not affect RB hyperphosphorylation (upper band tRB). **B.** LAPC4 PDR cells are sensitized to MEK inhibition, as analyzed via Trypan blue exclusion after 13 days treatment with 0.5 or 1μM U0126 or CTRL, whereas the parental cells are less responsive, indicating that the PDR cells have become more reliant on the MAPK activation.