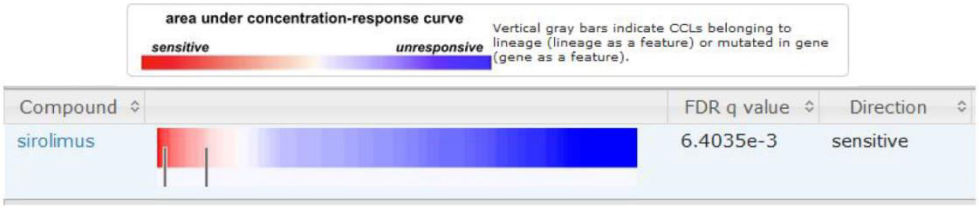
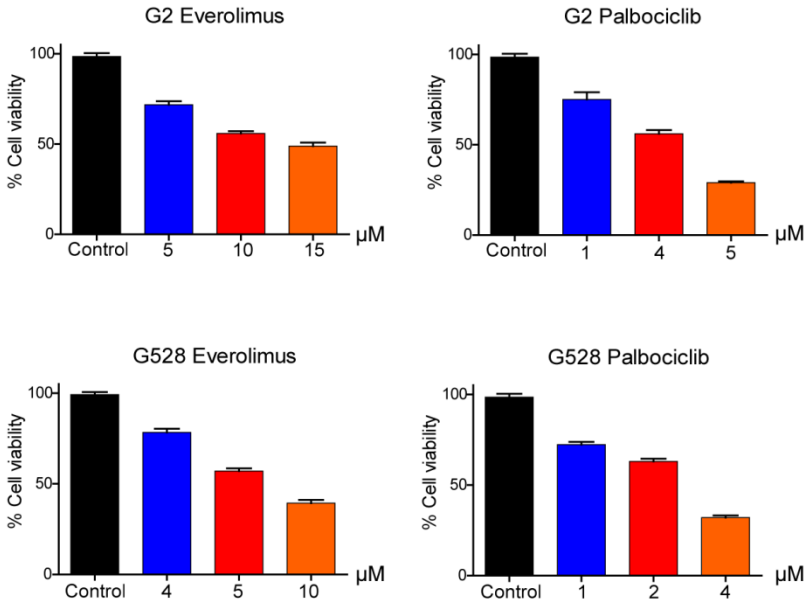
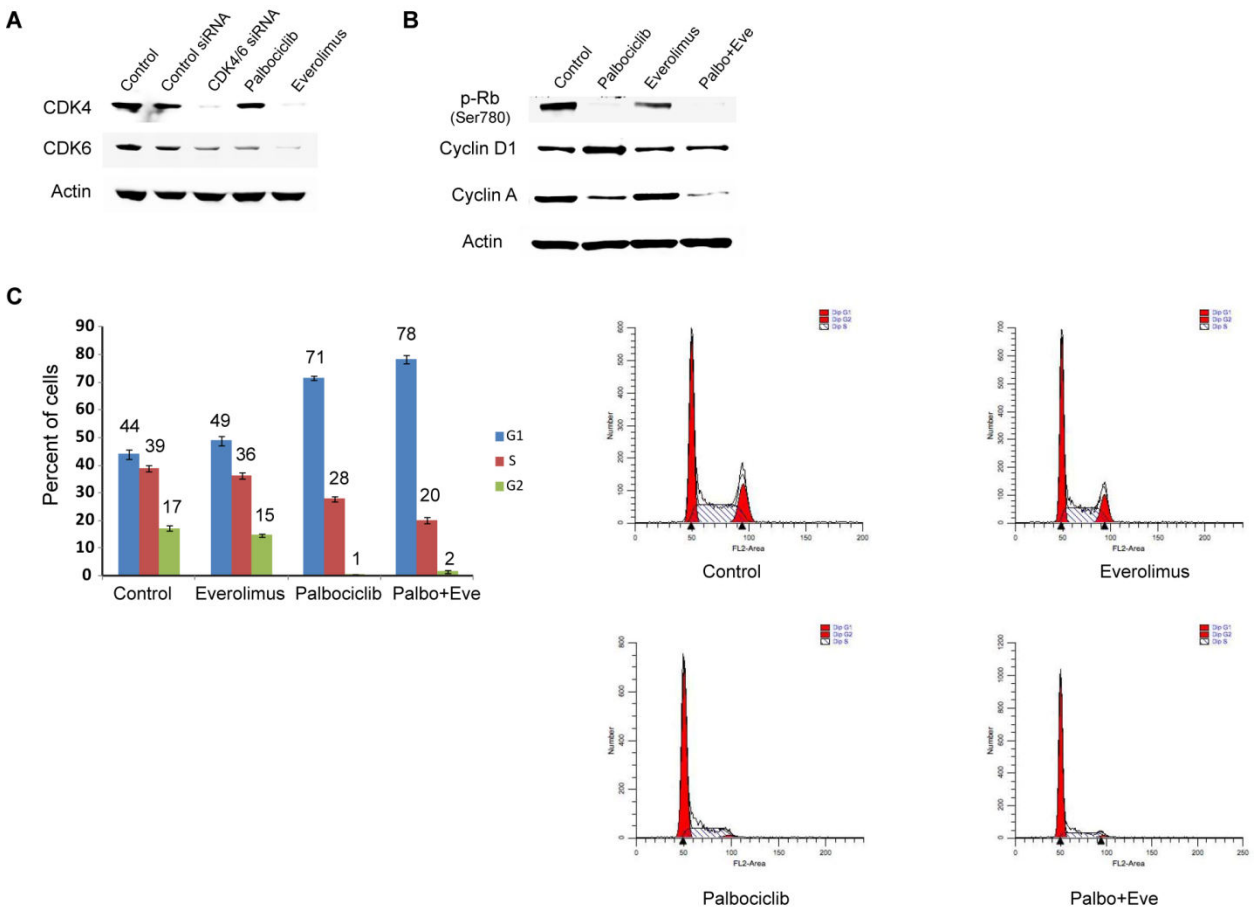


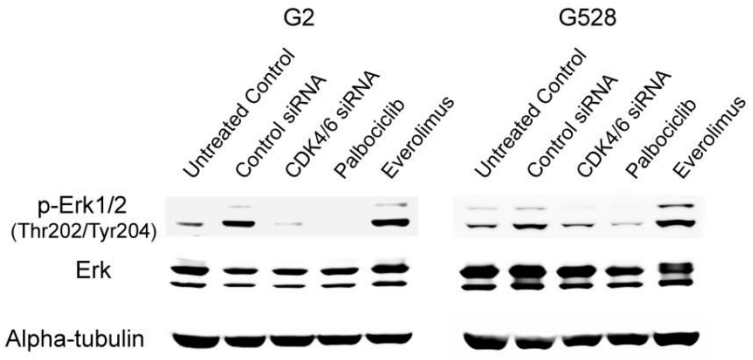
Supplementary Figure S1. Mutations in *CCND3* increase sensitivity to mTOR inhibition. Enrichment analysis showing increased sensitivity of cancer lines with mutations in *CCND3* to an mTOR inhibitor, sirolimus. Data are from the Cancer Therapeutics Response Portal (http://portals.broadinstitute.org/ctrp/).



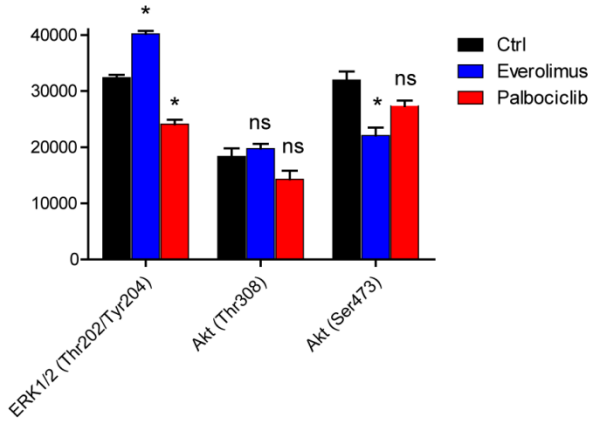
Supplementary Figure S2. Dose-response plots for everolimus and palbociclib. G2 and G528 lines show sensitivity to both palbociclib and everolimus in a dose-dependent manner.



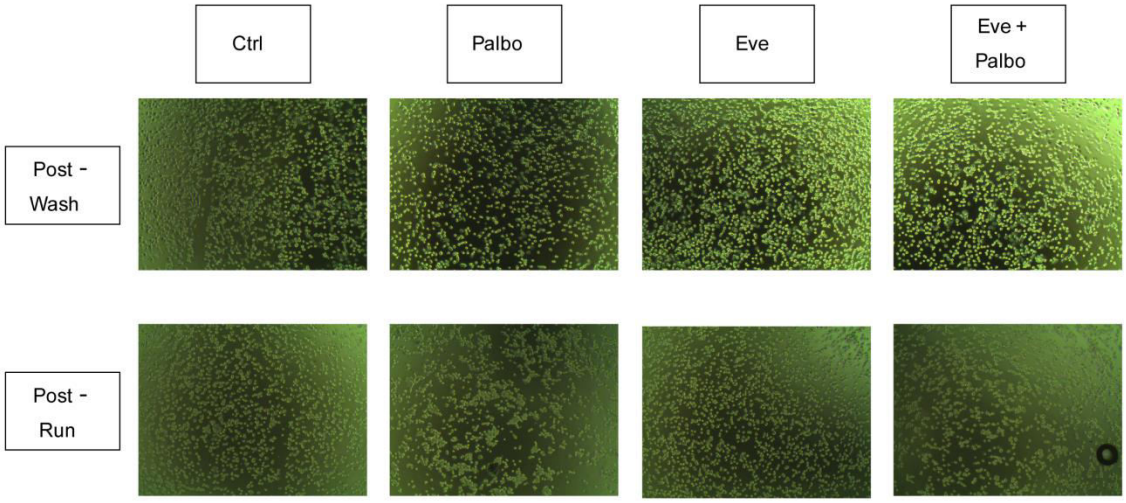
Supplementary Figure S3. mTOR inhibition with everolimus cross-regulates the CDK/Rb pathway. (**A-**B) Shown are immunoblots using specific antibodies for CDK4, CDK6, Cyclin D1, Cyclin A, and p-Rb. (**C**) Cell cycle analysis of G2 cells following 24 hours of treatment with palbociclib, everolimus, and the combination of both.



Supplementary Figure S4. Erk activity is linked to CDK4/6 inhibition. Shown are immunoblots using specific antibodies against p-Erk and Erk.

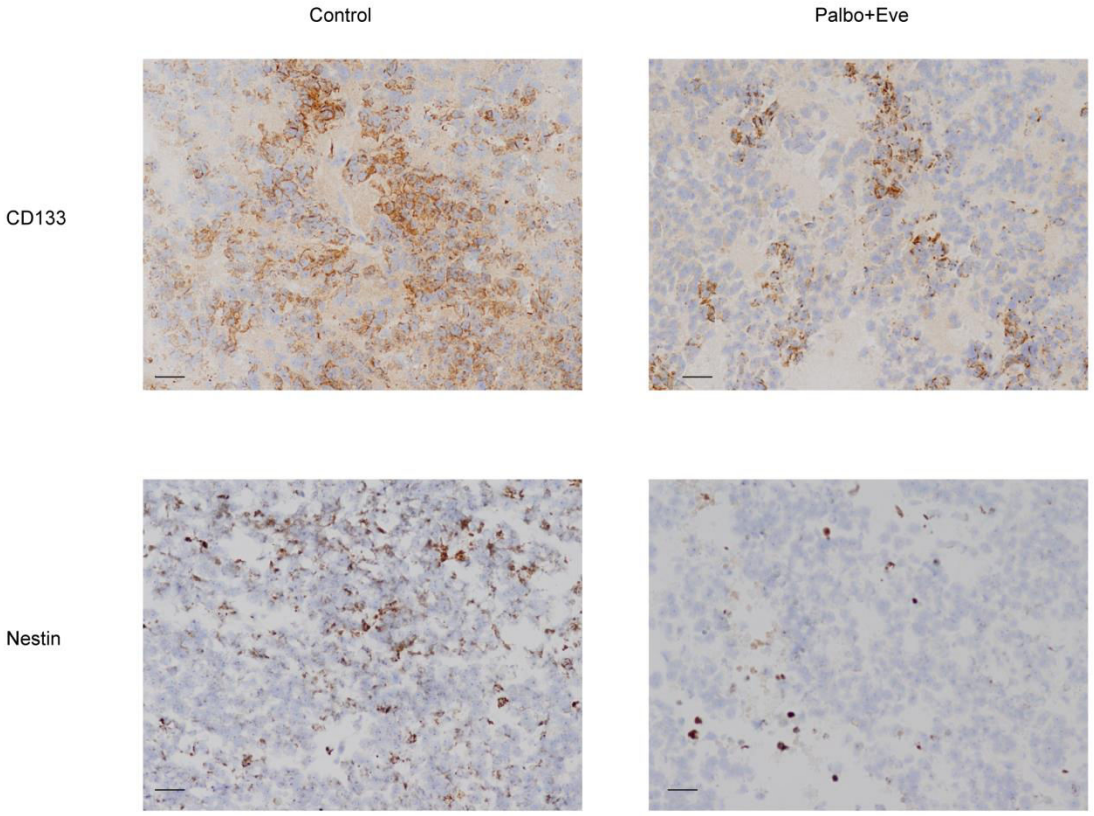


Supplementary Figure S5. Palbociclib treatment decreases the phosphorylation of Erk1/2. Antibody array (ELISA) results with antibodies specific for p-Erk, p-Akt (Thr308), and p-Akt (Ser473) are plotted (*P < 0.05; one-way ANOVA with post-hoc Tukey analysis. Values are mean ± SEM of triplicates).



Supplementary Figure S6. Cells remain attached throughout the Seahorse metabolic assays.

Shown are images taken after the washing processes and at the end of the metabolic assays.



Supplementary Figure S7. Immunohistochemistry staining of tumor harboring mouse brains for GIC markers. Both CD133 and nestin expression is less in the combination treatment group vs. control. Scale bar: 5 μm.