Figure S1. Schematic diagram for the computational approaches (see Appendix for detailed description).

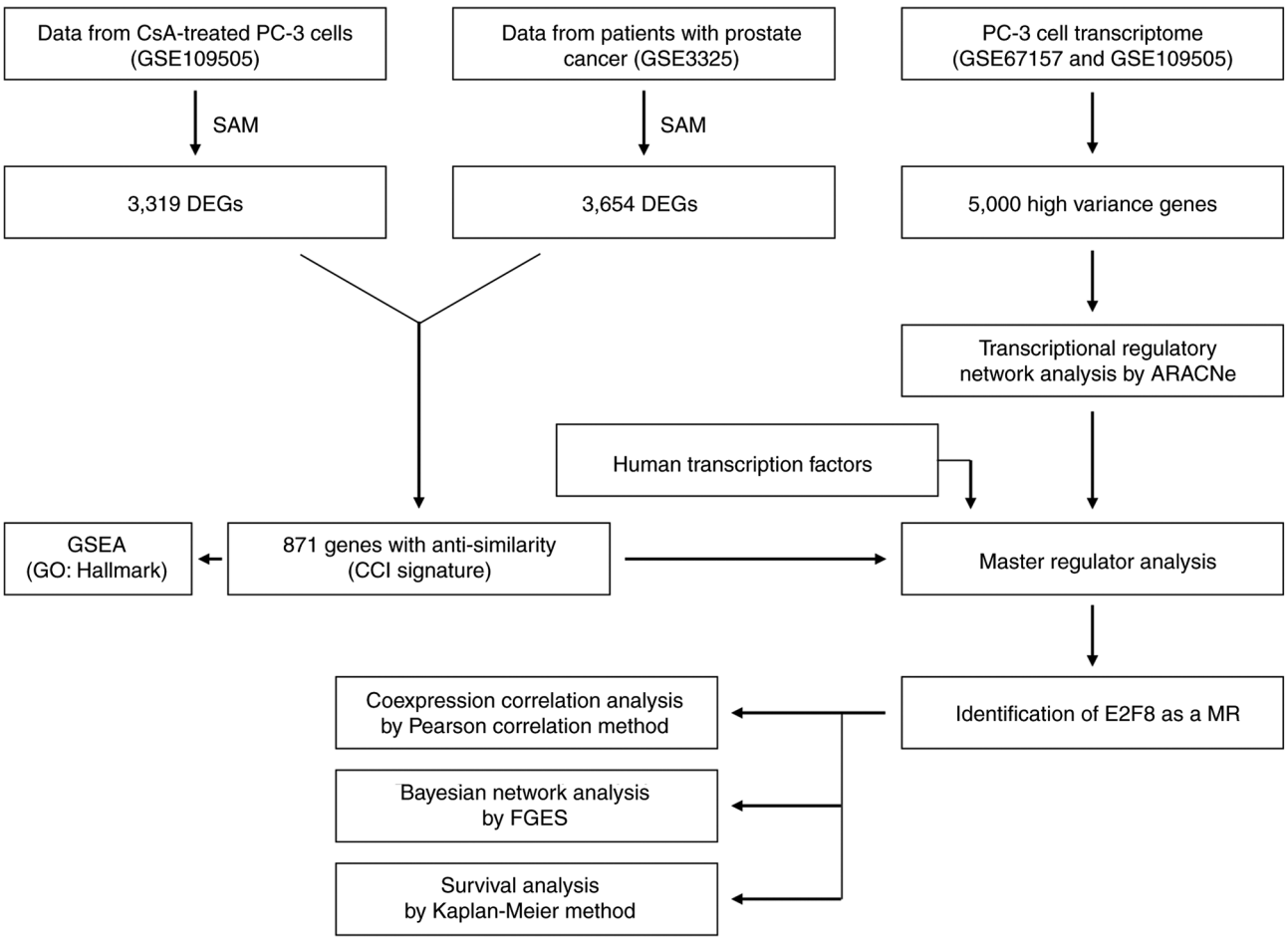

Figure S2. CsA induces a distinct gene expression profile. (A) Hierarchical clustering illustrates a large quantity of DEGs between vehicle- and CsA-treated PC-3 cells. The data were visualized using R 3.6.3 software (https://cran.r-project.org/src/base/R-3). (B) PCA plot shows distinct clusters between vehicle- or CsA-treated PC-3 cells. (C) Heatmap represents the CCI signature. The data were visualized using R 3.6.3 software (https://cran.r-project.org/src/base/R-3). (D) A total of 871 (593+278) DEGs show an inverse correlation between PC-3 cells treated with CsA and patients with metastatic prostate cancer. (E) Hallmark pathways related to the CCI signature. CsA, cyclosporin A; DEGs, differentially expressed genes; PCA, principal component analysis; CCI, clinically significant CsA-induced gene expression; V, vehicle.

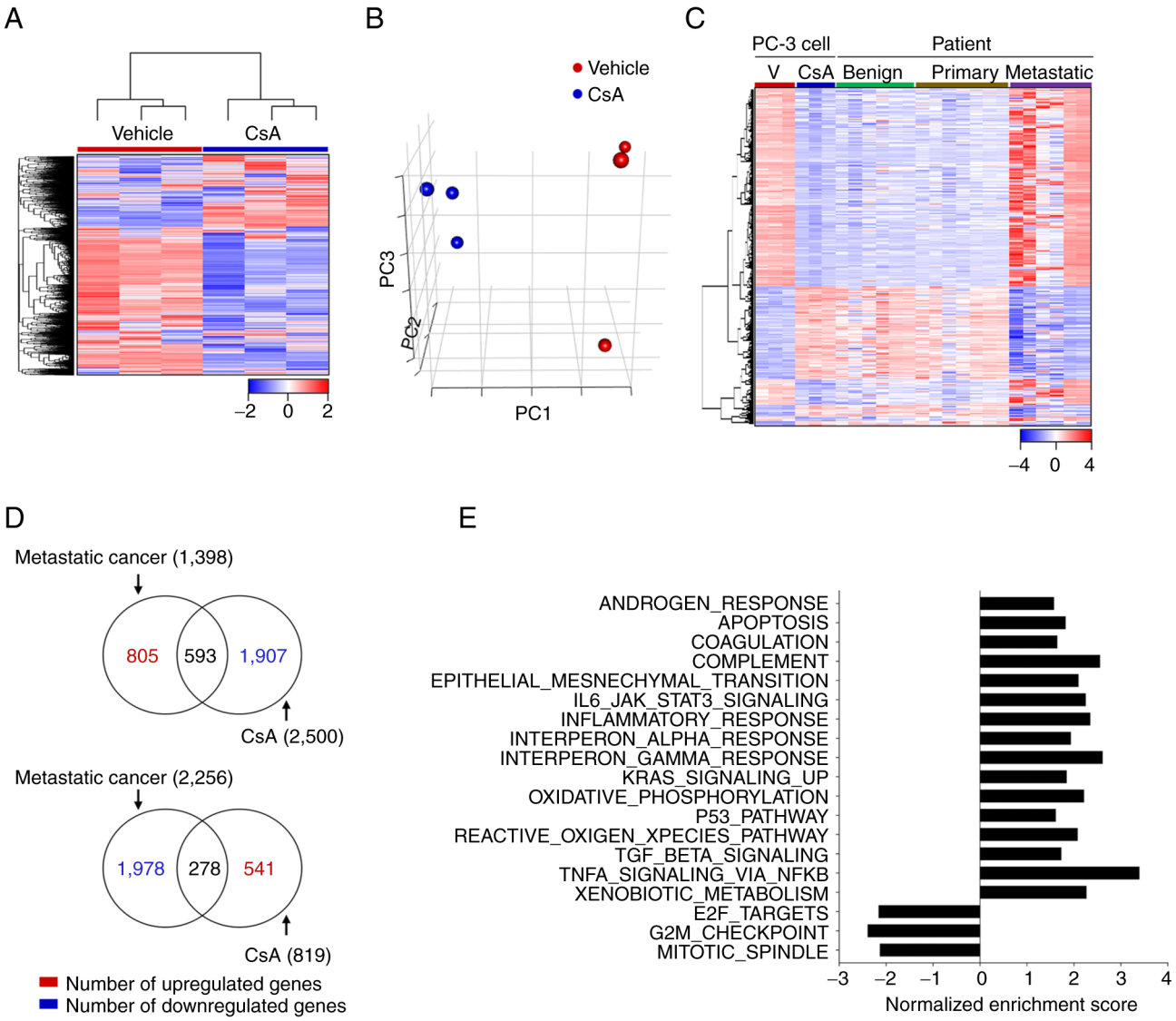

Figure S3. The biological pathways associated with the 216 E2F8 target genes. Bar chart illustrates NESs and log10 (*q*-value). NESs, normalized enrichment scores.

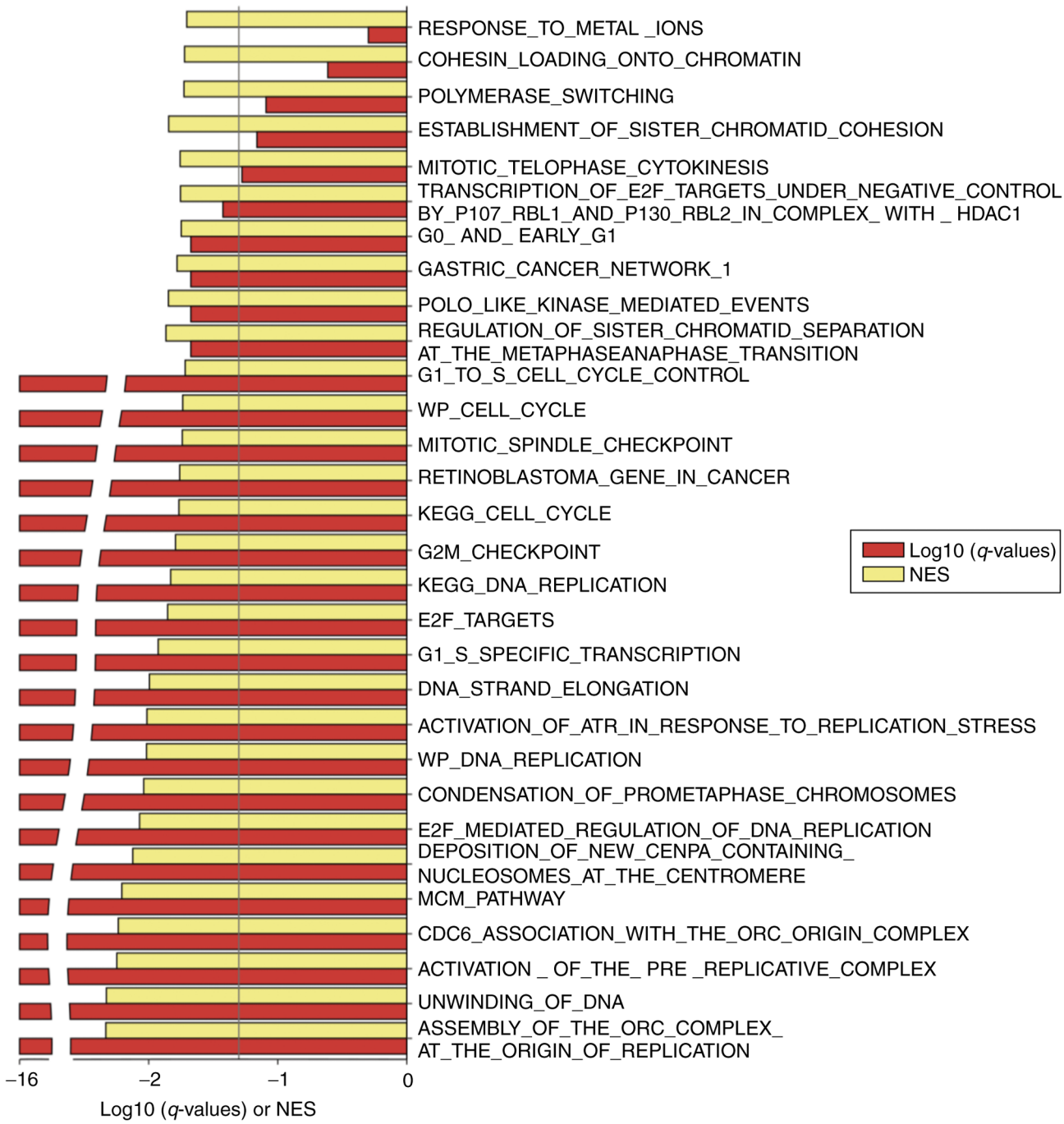

Figure S4. The expression of levels of MRs in GSE3325 (A) and GSE35988 (B). The x-axis indicates three different stages of prostate cancer and y-axis denotes the normalized expression levels. *P<0.05; **P<0.01; ***P<0.005; n.s., not significant. MRs, master regulators; B, benign prostate hyperplasia; P, primary tumor; M, metastatic tumor.

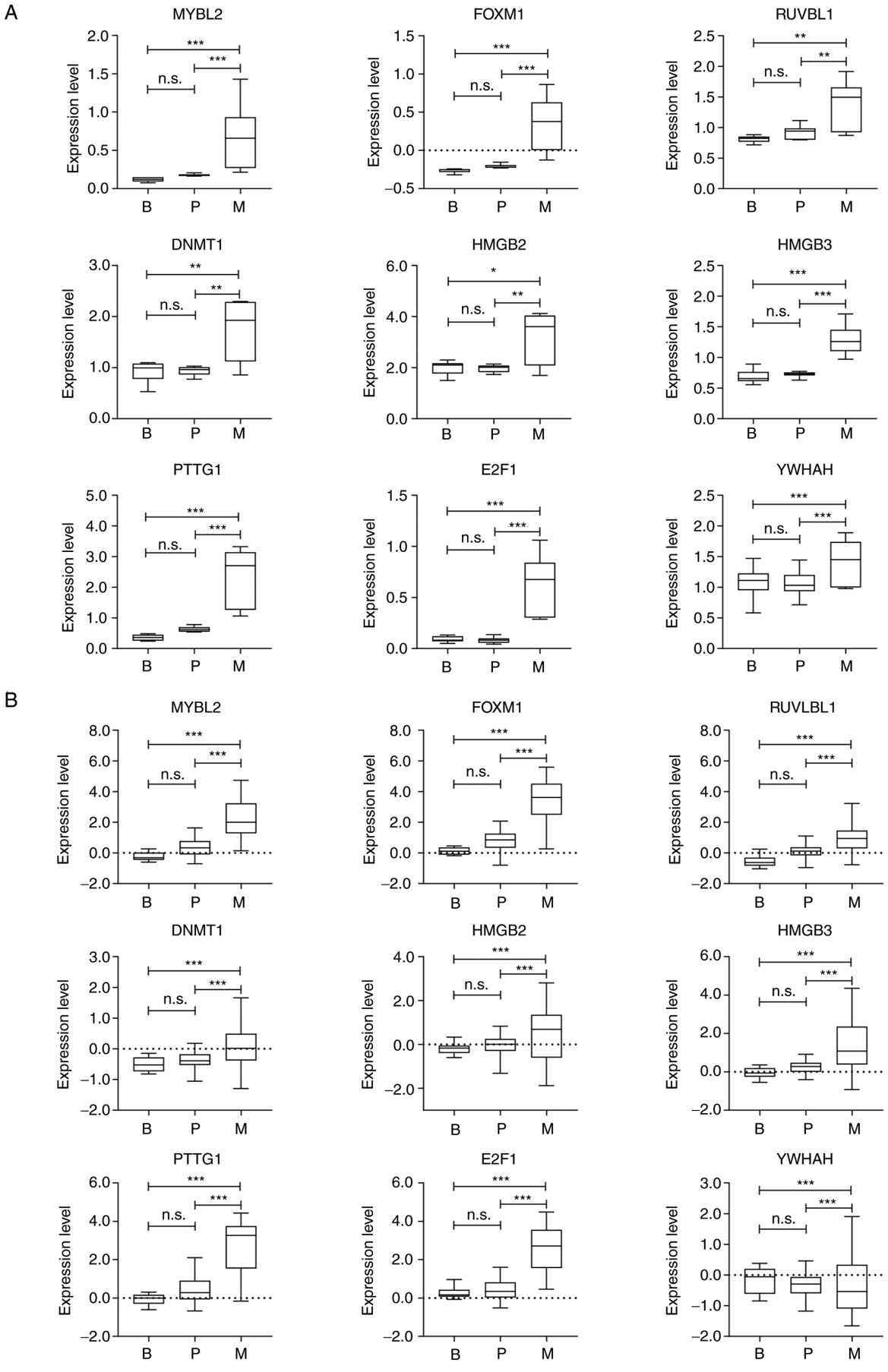

Figure S5. Overall survival for patients with prostate cancer based on the expression levels of MRs from cBioPortal transcriptomic data. (A) The Kaplan-Meier survival curves for patients with prostate cancer. (B) Hazard ratios and 95% confidence intervals are denoted in the graph. *P<0.05; **P<0.01; ***P<0.005. MRs, master regulators.

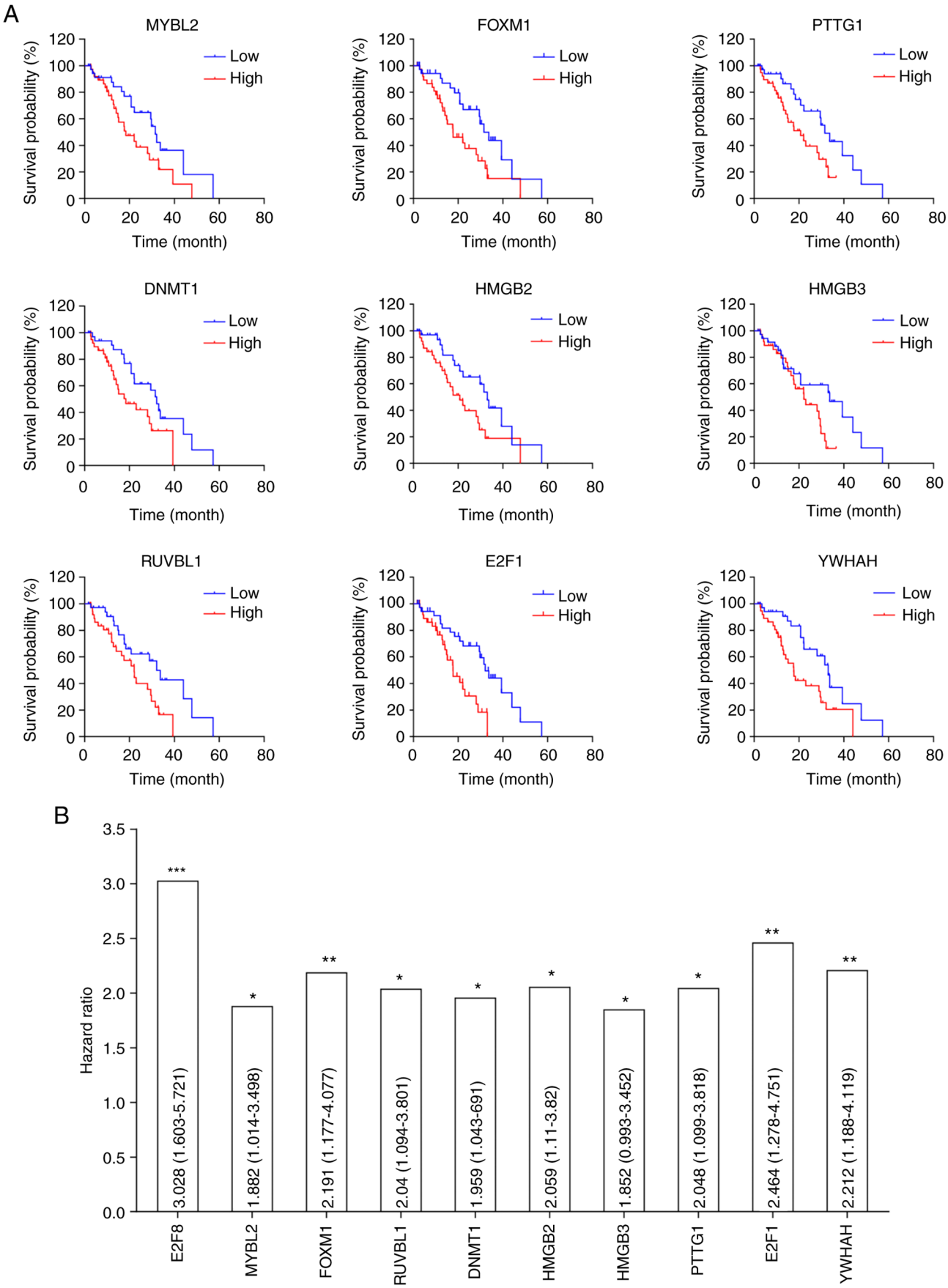

Figure S6. Real-time PCR and siRNA experiments. (A) The indicated cells were treated with 10 μM CsA for 48 h prior to real-time PCR analysis. The data were expressed as the mean ± SEM (n=6). ***P<0.005. (B) Each cell was transfected with 50 nM siE2F8-1 or siE2F8-2 for 48 h prior to western blot analysis. si, short interfering; CsA, cyclosporin A.

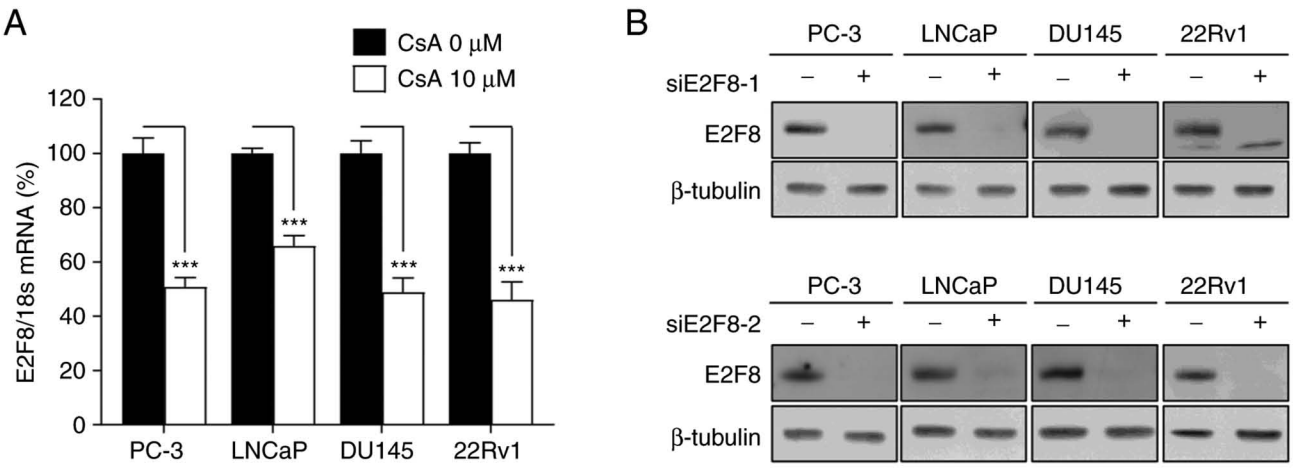

Figure S7. The role of MELK in prostate cancer cell growth. (A) Each cell was treated with 10 μM CsA for the indicated times prior to RT-PCR and western blot analysis. (B) The indicated cells were treated with 10 μM CsA for 48 h prior to real-time PCR analysis. The data were expressed as the mean ± SEM (n=6). n.s., not significant. (C) Each cell was transfected with 50 nM siMELK-1 or siMELK-2 for 48 h prior to MTT analysis. Cell growth was expressed as a relative value compared with that of siControl, which was set to 100%. The data were expressed as the mean ± SEM (n=4). **P<0.01; ***P<0.005. (D) Each cell was transfected with 50 nM siMELK-1 or siMELK-2 for 48 h prior to western blot analysis. CsA, cyclosporin A; si, short interfering.