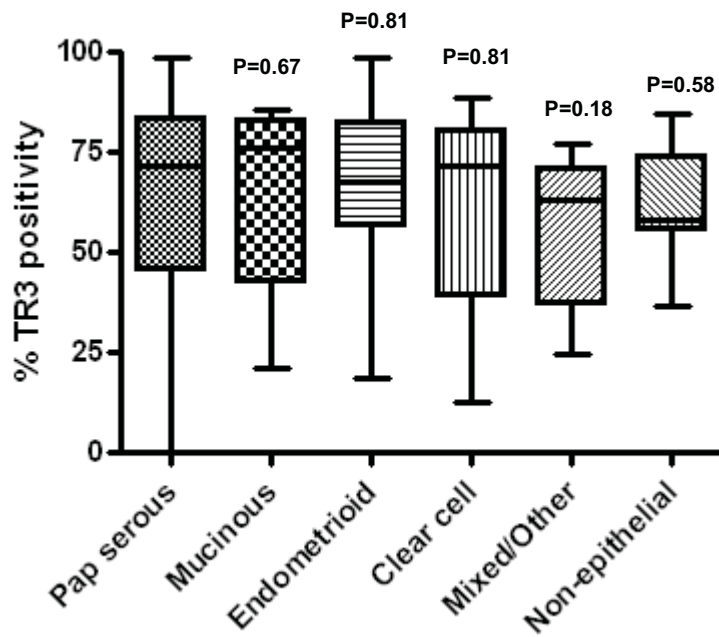


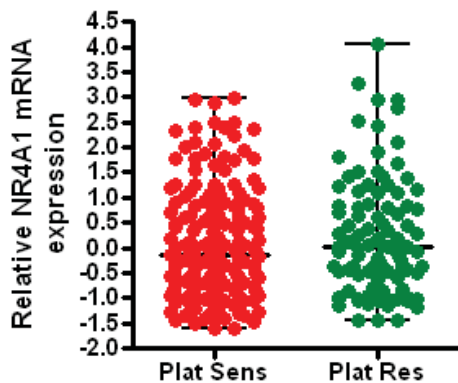
Supplementary Figure 1. TR3 expression in normal and neoplastic ovarian epithelium. (A) Representative low power photomicrographs of normal and neoplastic ovarian epithelium from human ovarian cancer patients undergoing surgical resection at Vanderbilt. Immunohistochemical analysis of TR3, the epithelial marker pan-cytokeratin and the proliferation marker Ki67 were performed. **(B)** High power photomicrographs of the boxed areas from (A).

A)

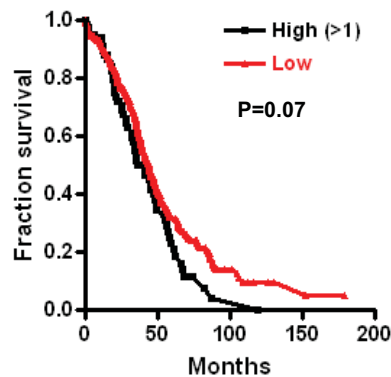


Supplementary Figure 2. Compared to epithelial papillary serous tumors, there were no significant differences in TR3 expression in other epithelial-derived tumors or non-epithelial tumors (Mann-Whitney test).

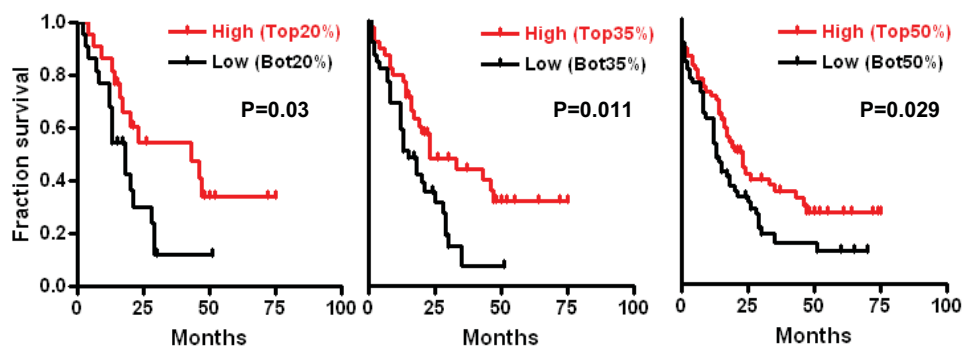
A) Platinum sensitivity-TCGA



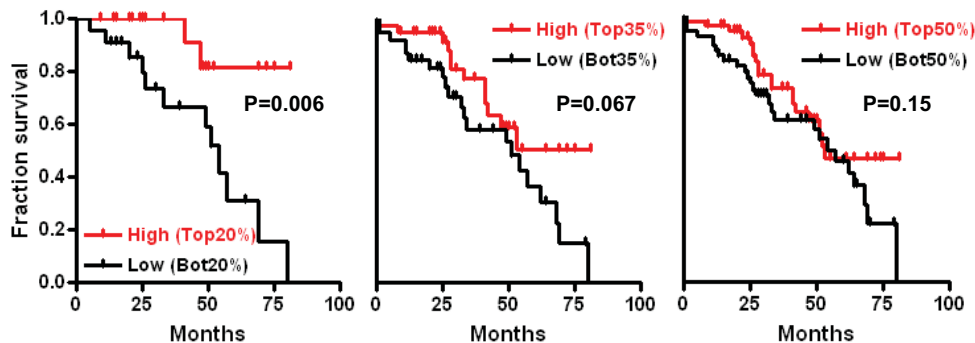
B) Overall survival-TCGA



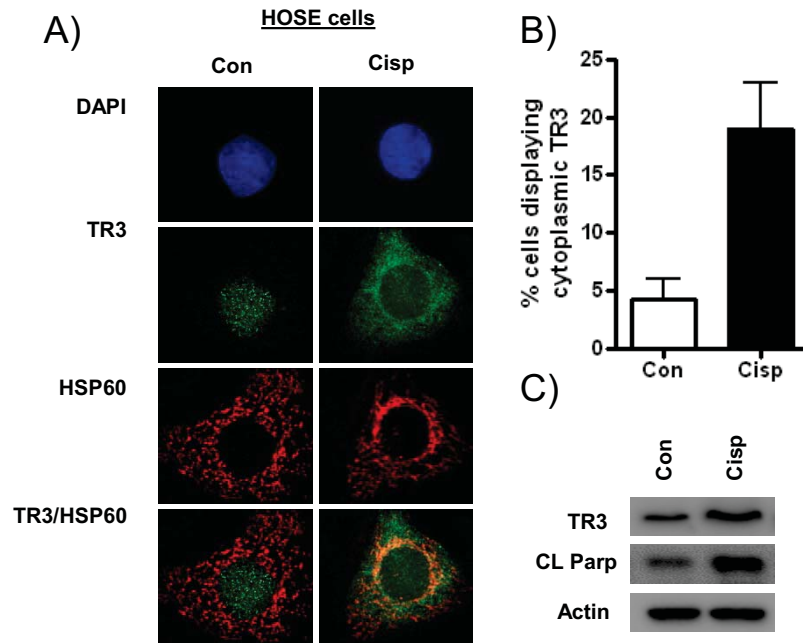
C) PFS



D) OS

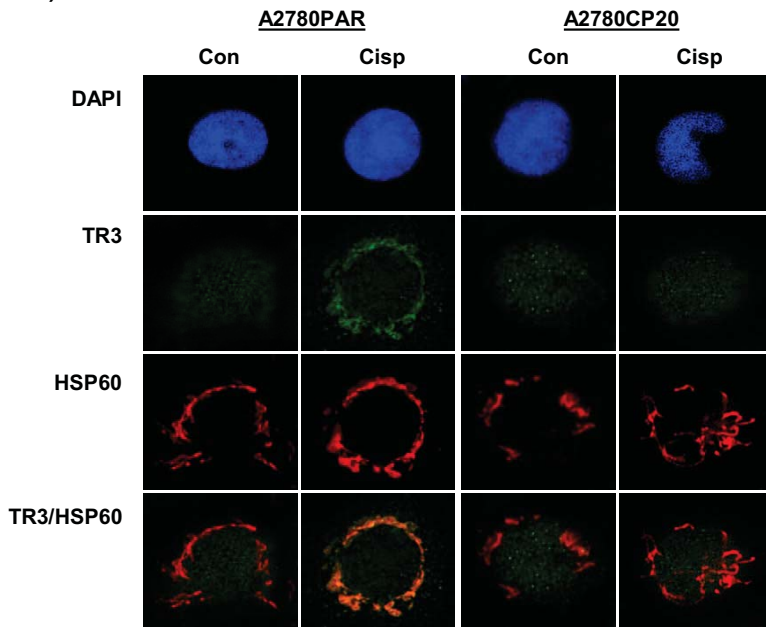


Supplementary Figure 3. Association of TR3 expression with clinical data in publicly available databases. TCGA data (ref 29 and data extracted from the TCGA Data Portal (<https://tcga-data.nci.nih.gov/tcga/>) of relative TR3 mRNA expression in tumors from 489 patients. Values shown are standardized Z scores of microarray data from 3 independent platforms. **(A)** Analysis of TR3 expression in platinum sensitive and resistant tumors. **(B)** Overall survival analysis in ovarian cancer patients with high (Z score > 1, representing at least 2-fold increase above expression in normal ovary) and low (Z score < 1) TR3 expression in tumors. P value shown is the likelihood ratio test. Yoshihara et al (ref 29) database of TR3 mRNA expression in serous ovarian tumors collected from 110 patients. Analysis of **(C)** progression-free survival and **(D)** overall survival in patients with top/bottom 20% (22 patients each), top/bottom 35% (39 patients each) and top/bottom 50% (55 patients each) expression of TR3 in tumors. P values shown are likelihood ratio test.

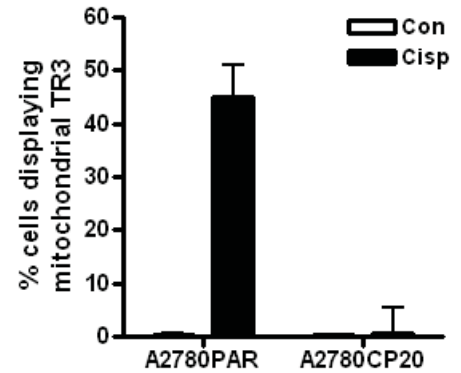


Supplementary Figure 4. Effects of cisplatin in normal HOSE ovarian epithelial cells. (A) Immunofluorescence analysis of subcellular TR3 localization in HOSE cells treated with cisplatin (5 μ M) for 24h. Representative photomicrographs of cells showing cytoplasmic localization of TR3 (green) in relation to DAPI-stained nuclei (blue) and mitochondrial Hsp60 (red) in cisplatin-treated-treated cells. **(B)** Percentage of cells displaying cytoplasmic TR3 targeting in cisplatin-treated cells. **(C)** Effects of cisplatin on protein expression of TR3 and cleaved PARP.

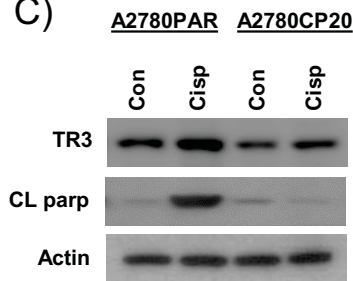
A)



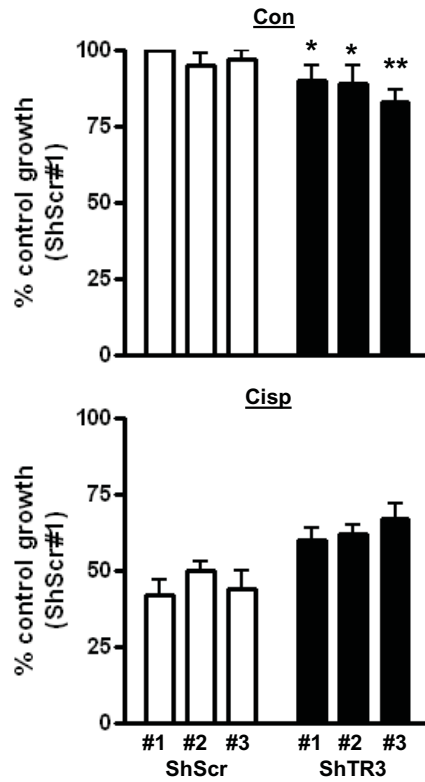
B)



C)

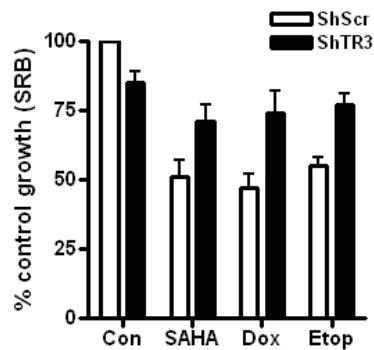


Supplementary Figure 5. Effects of cisplatin in A2780 PAR and CP20 ovarian cancer cells. (A) Immunofluorescence analysis of subcellular TR3 localization in cells treated with cisplatin (5 μ M) for 24h. Representative photomicrographs of cells showing cytoplasmic localization of TR3 (green) in relation to DAPI-stained nuclei (blue) and mitochondrial Hsp60 (red) in cisplatin-treated cells. **(B)** Percentage of cells displaying mitochondrial TR3 targeting in cisplatin-treated cells. **(C)** Effects of cisplatin on protein expression of TR3 and cleaved PARP.

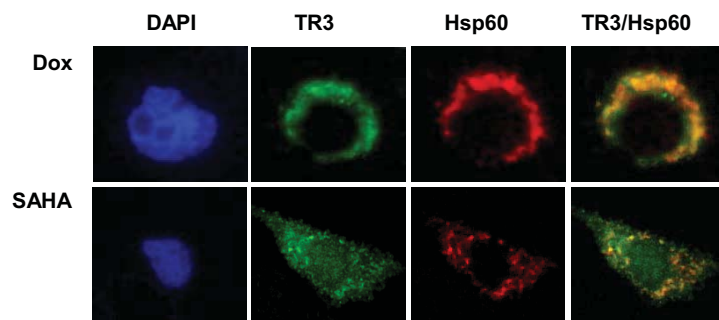


Supplementary Figure 6. The effect of cisplatin (5 μ M) on cell growth and cytotoxicity in SRB assays in OVCAR8 ShScr and ShTR3 cells (72h treatment). Values are the percentage of control (ShScr#1) growth (mean + SD of 3 independent experiments). * $p < 0.05$ relative to ShScr#1; ** $p < 0.02$ relative to ShScr#1, #2 and #3, Student's t test).

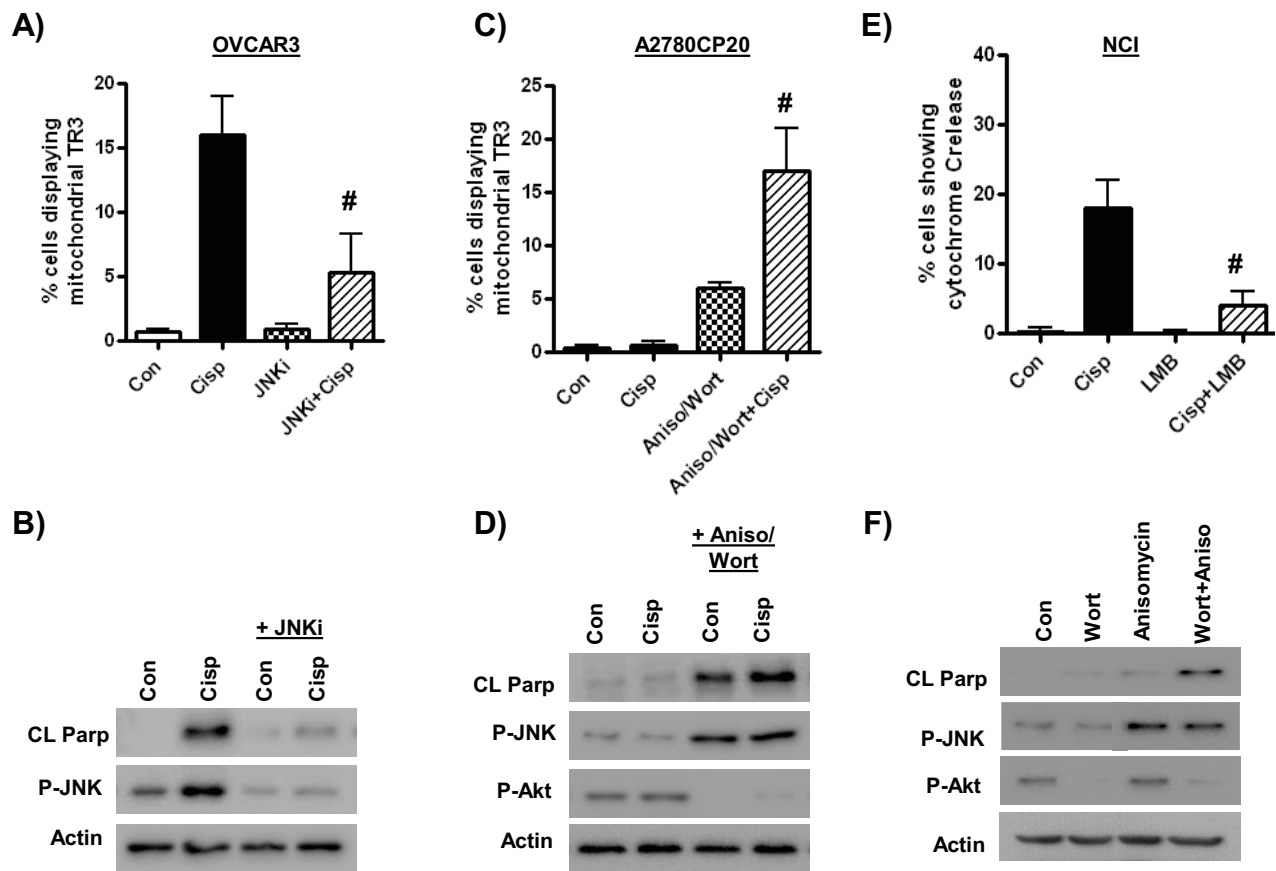
A)



B)



Supplementary Figure 7. Effects of doxorubicin and the histone deacetylase inhibitor SAHA are inhibited by TR3 down-regulation. (A) The effect of doxorubicin (0.5 μM) and SAHA (5 μM) on ShScr and ShTR3 cell growth and cytotoxicity in SRB assays (72h treatment). Values are the percentage of control (ShScr) growth for each drug tested. Values are mean + SD of 3 independent experiments. **(B)** Immunofluorescence analysis of subcellular TR3 localization in OVCAR8 cells treated with doxorubicin (0.5 μM) or SAHA (5 μM) for 24h. Representative photomicrographs of cells showing cytoplasmic localization of TR3 (green) in relation to DAPI-stained nuclei (blue) and mitochondrial Hsp60 (red) in drug treated-treated cells.



Supplementary Figure 8. Effects of 2h pre-treatment and then co-treatment with the JNK inhibitor SP600125 (20 μ M) on **(A)** mitochondrial localization of TR3 and **(B)** protein levels of cleaved PARP and phospho-JNK (Thr183/Tyr185) in cisplatin-treated OVCAR3 cells (5mM; 24h). Effects of 2h pre-treatment and co-treatment (3 hourly pulses) with the JNK activator anisomycin (25 ng/ml) and Akt inhibitor wortmannin (5 μ M) on **(C)** mitochondrial localization of TR3 and **(D)** protein levels of cleaved PARP, phospho-JNK (Thr183/Tyr185) and phospho-Akt (Ser473) in cisplatin-treated A2780 CP20 cells (5 μ M; 12h). The effects of 2h pre-treatment and co-treatment (3 hourly pulses) with wortmannin (5 μ M), anisomycin (25 ng/ml) or the combination in NCI/ADR-RES cells on **(E)** TR3 localization and **(F)** protein levels of cleaved PARP, phospho-JNK (Thr183/Tyr185) and phospho-Akt (Ser473) (12h treatment). Values are mean + SD of 3 independent experiments. # $p < 0.01$ relative to cisplatin alone Student's t test.