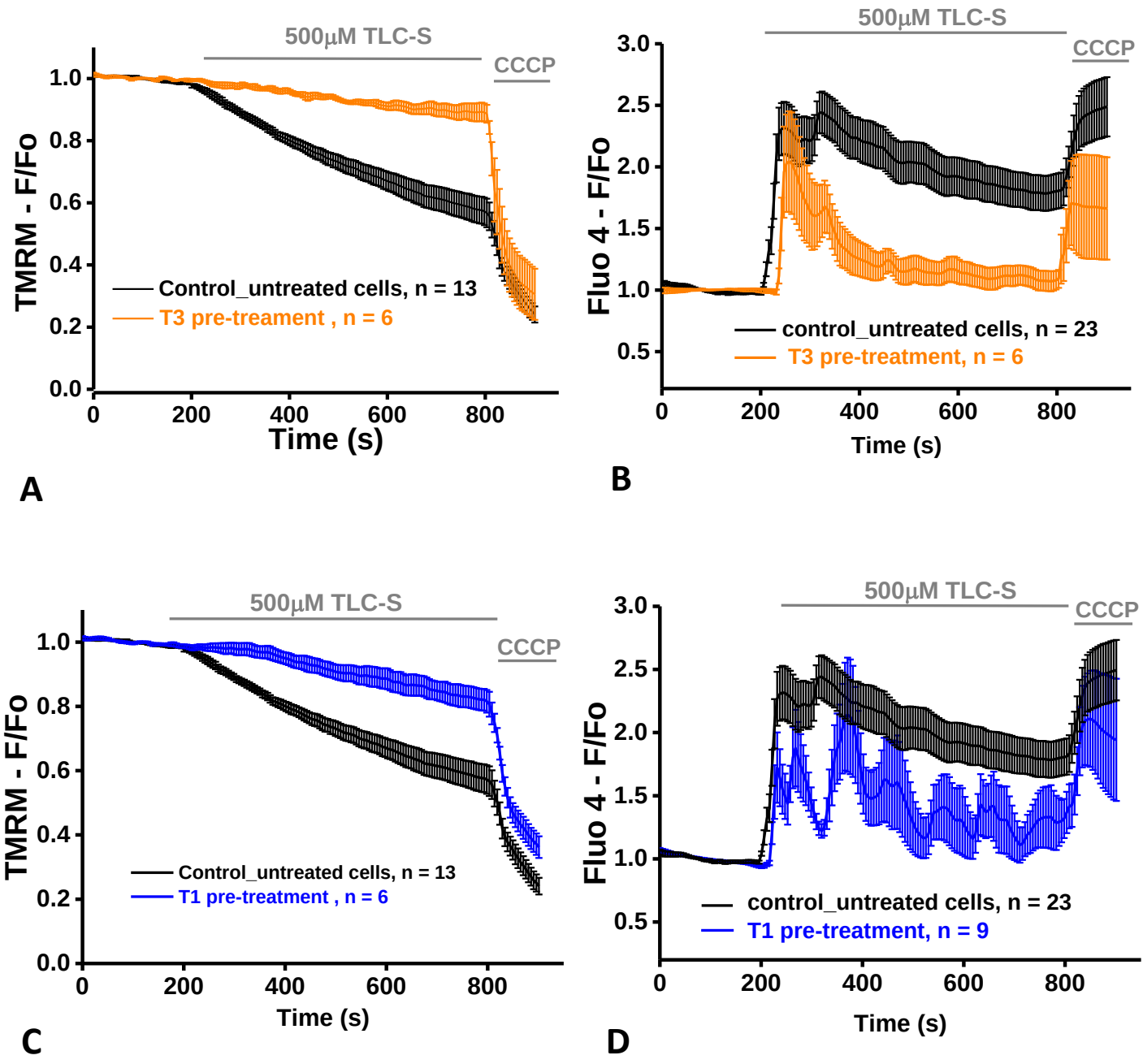
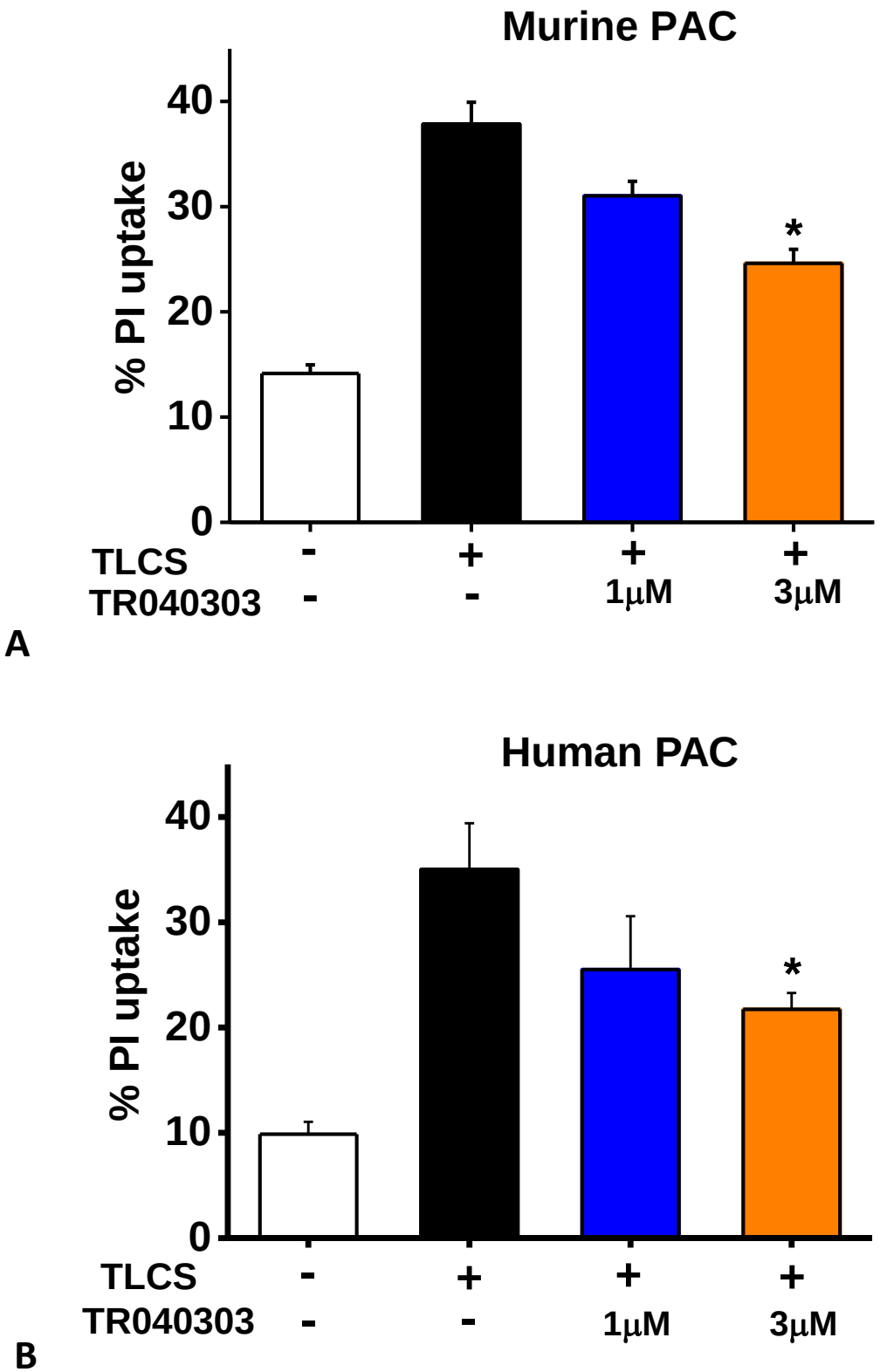
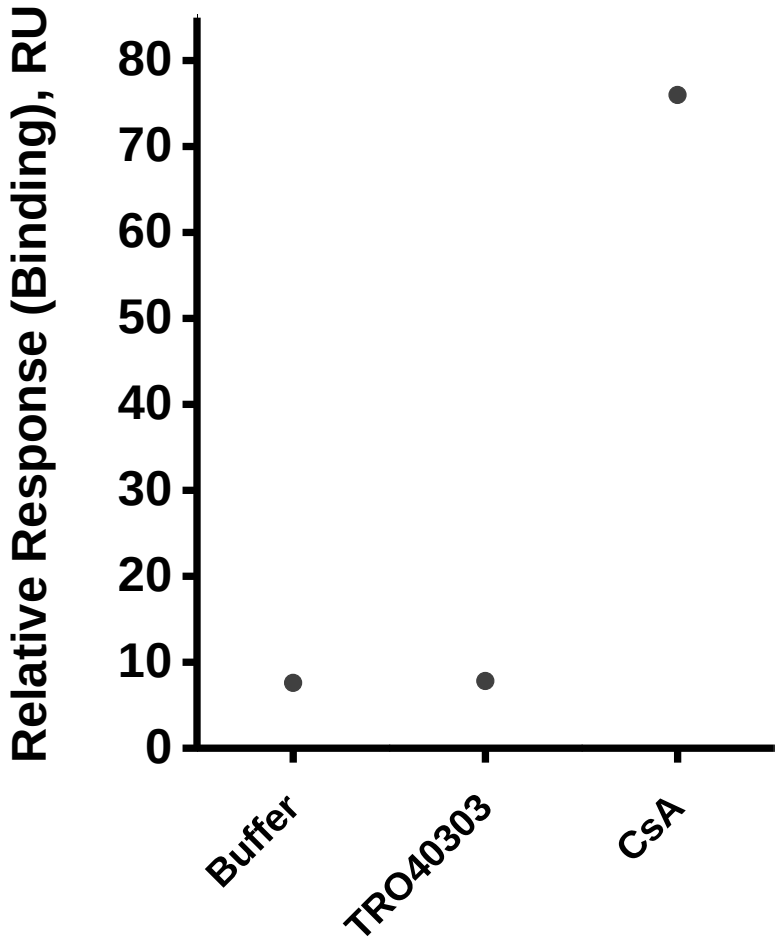


SUPPLEMENTAL FIGURE 1. TRO40303 reduced loss of mitochondrial membrane potential ($\Delta\psi_m$) and overload of $[Ca^{2+}]_c$ in freshly isolated murine pancreatic acinar cells (PACs; confocal fluorescence; mean ± s.e.m. ratio to basal, F/F_0). A, Taurolithocholic acid sulphate (TLCS, 500 µM) induced falls in $\Delta\psi_m$ (tetramethyl rhodamine methyl ester, TMRM) and (B) large elevations in $[Ca^{2+}]_c$ (Fluo-4); positive control, protonophore carbonyl cyanide m-chloro phenyl hydrazone, CCCP). Pre-treatment with TRO40303 (3 µM = T3) decreased the extent of depolarisation, preserving $\Delta\psi_m$. Pre-treatment with T3 did not affect the initial rise in $[Ca^{2+}]_c$ but reduced overload of $[Ca^{2+}]_c$ during the plateau phase. C, Although a lower concentration of TRO40303 (1 µM = T1) protected against loss of $\Delta\psi_m$, (D) the effect on $[Ca^{2+}]_c$ was less pronounced .



SUPPLEMENTAL FIGURE 2. TRO40303 reduced necrotic cell death pathway activation in freshly isolated murine and human pancreatic acinar cells (PACs). Taurolithocholic acid sulphate (TLCS, 500 μM) induced necrotic cell death pathway activation indicated by propidium iodide (PI) uptake. Pre-treatment with TRO40303 (3 μM, T3 or 1 μM, T1) reduced necrotic cell death pathway activation in (A) murine and (B) human PACs, an effect that was concentration dependent (TLCS vs TLCS plus TRO40303, *$P < 0.05$).



SUPPLEMENTAL FIGURE 3. Surface plasmon resonance demonstrated no binding affinity of TRO40303 with cyclophilin D (Cyp-D). Experiments were performed by the addition of 100µM TRO40303 over recombinant Cyp-D immobilized on a CM5 sensor chip. TRO40303 resulted in the same response as buffer. Cyclosporine A (CsA), which has a strong binding affinity for Cyp-D, was used as a positive control. TRO40303 showed no binding with Cyp-D.