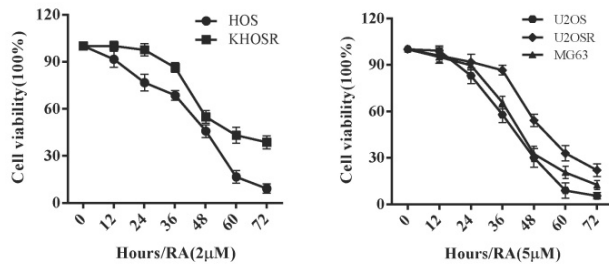
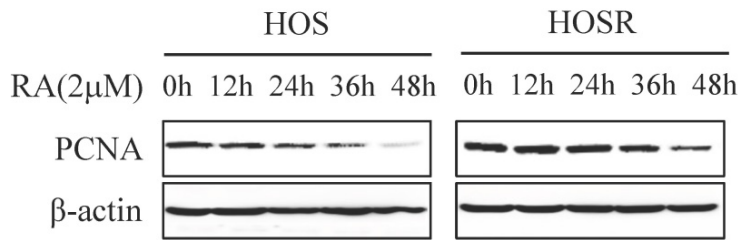


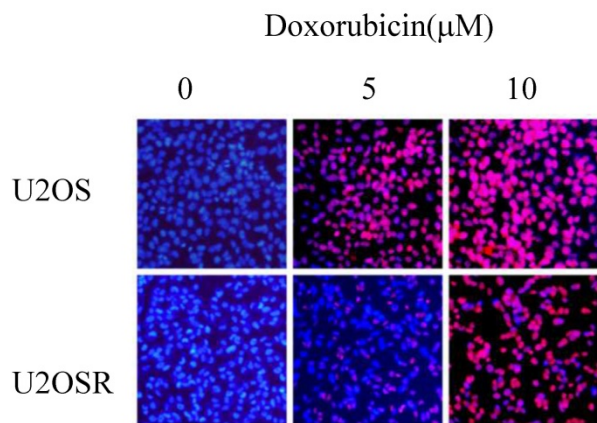
a



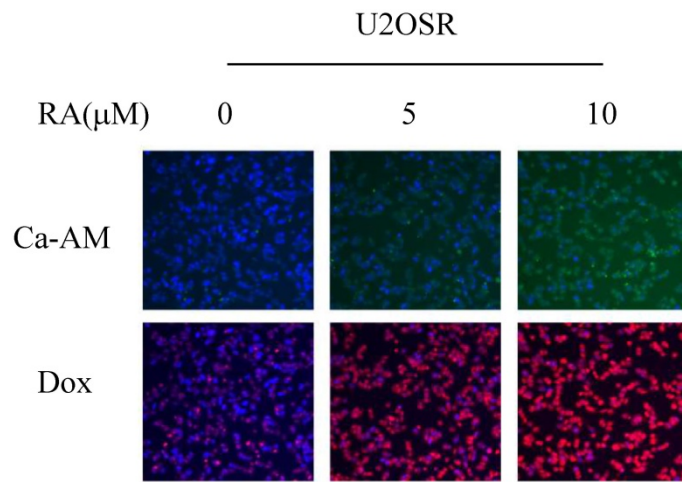
b



Supplementary Fig. 1 RA inhibits cell viability in a time-dependent manner. (a) The cell lines were treated with RA of the indicated concentration for 0 to 72 h, and the cell viability were detected every 12 h using the CCK8 assays. (b) After RA (2 μM) treated for a serial time, the expression of PCNA was detected by WB in osteosarcoma cells.



Supplementary Fig. 2 Drug-resistant cell inhibits doxorubicin uptake. Cells were treated with doxorubicin (0, 5, and 10 μM) for 2 h in U2OS and U2OSR, and cell nuclei were stained by DAPI (blue). Images were acquired with a fluorescence microscope (Leica).



Supplementary Fig. 3 RA decreases calcein AM efflux and increases doxorubicin uptake. The intracellular calcein AM were hydrolyzed to fluorescent calcein (green) by intracellular esterase. Pretreated with RA (0, 2, and 5 μ M) for 24 h in cells, calcein AM was used to indicate the physical change of efflux, and doxorubicin were used to detect the physical changes of uptake. Cell nucleuses were stained by DAPI (blue). Images were acquired with a fluorescence microscope (Leica). The fluorescence could be quantified by SpectraMax[®] M5/M5e plate reader.