**Strategy to enhance the therapeutic effect of doxorubicin in human hepatocellular carcinoma by selenocystine, a synergistic agent that regulates the ROS-mediated signaling**

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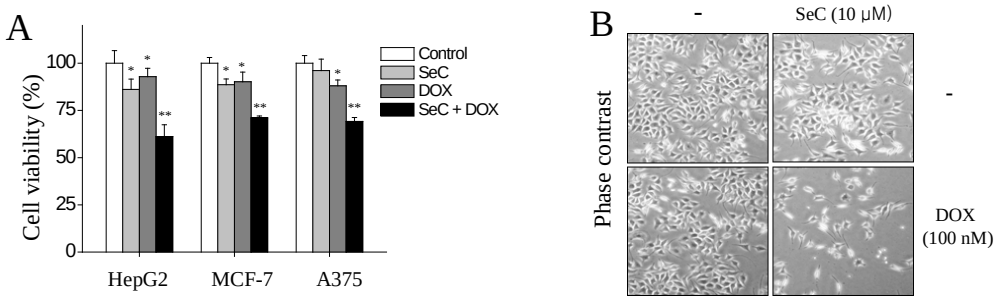


**Figure S1. Cytotoxicity of SeC and DOX towards human cancer cells. A**. Combined treatment-induced growth inhibition against human cancer cells. The cells exposed to 8 μM SeC for 24 h were co-incubated with 100 nM DOX for 24 h. Cell viability was determined by MTT assay. **B**. Changes of cell morphology. HepG2 cells after treatment with SeC (10 μM) or/and DOX 100 nM were observed by phase contrast microscope (Magnification, 200×). All data here are expressed as means ± SD of triplicates. The image shown here is representative of three independent experiments with similar results.

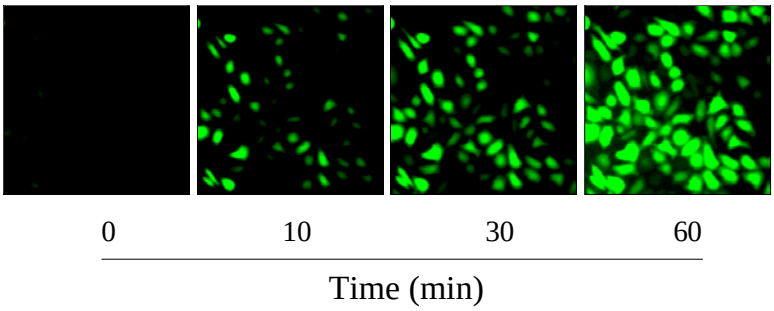


**Figure S2. SeC induces time-dependent intracellular ROS accumulation.** HepG2 cells were treated with 10 μM SeC for 0, 10, 30 and 60 min and then imaged by fluorescence microscope (magnification, 200×). The image shown here is representative of three independent experiments with similar results.

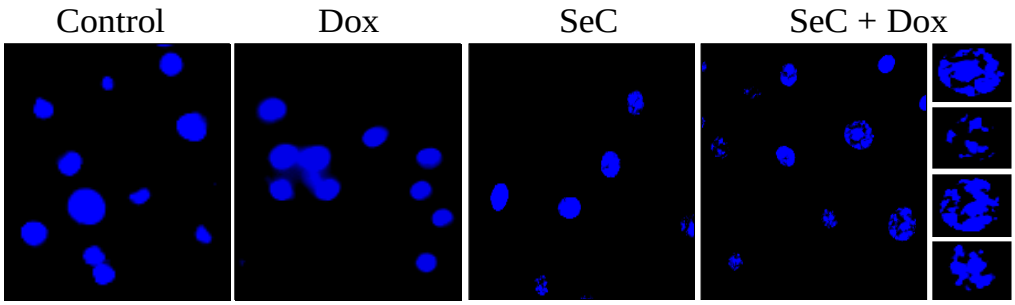


**Figure S3. SeC enhances Dox-induced DNA damage.** HepG2 cells cultured in chamber slides were pretreated with 10 μM SeC for 24 h and co-treated with Dox for 24 h. Then cells were fixed with 3.7% formaldehyde for 10 min and incubated with 1 μg/ml of DAPI for 15 min at 37℃. The cells were then washed with PBS and examined under a fluorescence microscope (magnification, 200×). The image shown here is representative of three independent experiments with similar results.

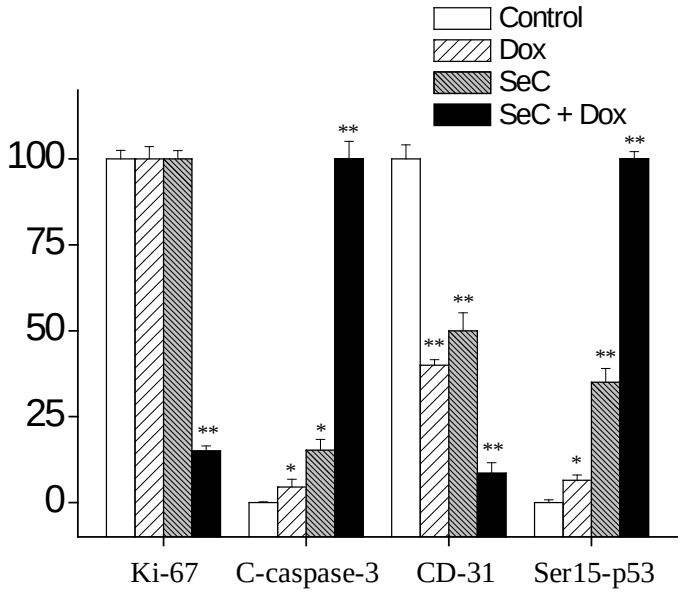


**Figure S4. Statistic analysis of proteins expression *in vivo.*** The protein expression was examined by IHC methods and analysed by Leica QW550 software. All data here are expressed as means ± SD of triplicates