Suppl Fig 1. Toxicology studies of DPS in mouse. Nude mice were treated with DPS (100 mg/kg, IP, 3 times/wk). A2, Nude mice were treated with DPS (100 mg/kg, IP) once with or without total body irradiation (XRT, 6 Gy). Arrows indicate the days of DPS treatment. The body weight was measured 3 times/wk. The weight was normalized with initial body weight (BW). The histology of liver, heart, stomach, kidney, intestine, and spleen were also examined and observed no apparent pathological abnormalities, as reported in Reference (18) with this dose level of DPS.

Suppl Fig 2. DPS did not induce autophagy in HI-LAPC-4 cells. Cells were treated with DPS or STF-62247 (STF, 2 μM, positive control) (1) at indicated concentrations and times. Panel A includes representative micrographs of untreated cells and cells treated with DPS or STF. B, cells were treated by DPS (9 μM, 24 hr) and STF (2 μM, 15 hr) and analyzed by Western blot for autophagy marker LC-3b cleavage. STF-62247, but not DPS, treatment led to morphological changes (vacuole formation) and LC-3 activation, suggesting autophagy was not involved in DPS- induced cell death.


Suppl Fig 3. DPS did not induce cell cycle arrest. HI-LAPC-4 cells were treated with DPS at indicated concentrations for 4 hrs and then used immediately (0 hr) or maintained for 24 hr (24 hr) before cell cycle analysis. Irradiation (20 Gy, under NO) and Bleomycin (40 μM, under HO) was used as positive controls for inducing DNA damage and G2/M cell cycle arrest. A, Representative histograms of flow cytometry; B, quantified data of G2/M phase cell, and expressed as the % in total cell population.

For the Cell cycle analysis, cells were fixed with 50% ice-cold ethanol overnight at 4°C, and treated with RNase A (5 mg/mL, 30 min) and then PI (1 mg/mL, 10 min) at room temperature, and quantified by flow cytometry.
Suppl Fig 4. DPS did not enhance IR-induced DNA damage. Subconfluent HI-LAPC-4 cells were treated with DPS (3 M, 4.5 hr) and/or irradiation (IR, 5 Gy). The IR was given either 0.5 or 4.5 hr before the end of the DPS treatment. After the treatment, cells were either collected immediately (A), or maintained in fresh media for 12 hr before collection (B). The DNA damage was assessed by γ-H2Ax western analysis.

Suppl Fig 5. DPS activity on solid tumor cells was not dependent on mitochondrial damage. Subconfluent cells were placed under normoxia (NO) and hypoxia (HO, 0.5%), and treated with DPS for 4 hr (A, 10 μM) or 8 hr (B). A, mitochondria membrane potential (MMP) measurement by fluorescent probe JC-1 using flow cytometry. B, mitochondrial superoxide measurement by FACS. *, P < 0.05 and §, P < 0.01 for comparison with untreated control by Student t-test. H₂O₂ (10 mM, 10 min) was used as the positive control in A, and rotenone (1.5 μM, 8 hr) used as the positive control in B.

Suppl Fig 6. DPS cytotoxicity depends partially on protein synthesis. HI-LAPC-4 cells were incubated with cycloheximide (CHX, 10 μM) for 0.5 hr before treatment with DPS (9 μM) and CHX (10 μM) under normoxia and hypoxia (0.5% O₂) for 4 hr. Cells were then maintained in fresh medium for 3 more days before MTT assay. *, P < 0.0001 for interaction of DPS and CHX by two-way ANOVA analysis, indicating that CHX inhibits DPS effect.

Suppl Fig 7. JNK was activated by DPS, but not required for DPS cytotoxicity. A, HI-LAPC-4 cells were treated with DPS at indicated times, and analyzed by Western blot for total and phosphorylated JNK. B-D, HI-LAPC-4 cells were pre-treated with JNK inhibitor SP 600125 (SP, Calbiochem) for 30 min, and incubated with DPS in the presence of SP for 24 hr (B, NO and HO), 8 hr (C, NO), and 48 hr (D, NO) before MTT assay. SP10 and SP50, treatment with SP 600125 10 μM and 50 μM, respectively. NO, normoxia; HO, hypoxia; CON, untreated control.
**Suppl Fig 8. DPS did not modulate HIF1α protein and transcriptional activity.** A, HI-LAPC-4 cells were treated under normoxia (NO) and hypoxia (HO, 0.5% O2) for 24 hr (A1) or 0.5 to 4 hr (3 μM, A2), and the expression of HIF1α and β-actin was measured by western blot. B, HIF1α target gene expression [VEGFα, hexokinase 2 (HK2)], and HIF2α were measured by RT-qPCR after 4 hr treatment with DPS in NO and HO. The methods and primer sequences used are presented at Suppl Table 4B.

**Suppl Fig 9. Oncogene RAS and MYC were overexpressed in HI-LAPC-4 and PC-3 cancer cells.** Human prostate-derived fibroblasts (HF) were compared with HI-LAPC-4 and PC-3 cells for c-Myc and RAS (total and activated) by Western blot. For RAS activity analysis, the activated (GTP-bound) RAS was isolated by GTP-RAS binding peptide (MilliPore RAS activation Kit, Cat#: 17-218). The remaining RAS after peptide-coated beads pull-down (supernatant) was used for assessment of total (GTP- and GDP- bound RAS).