Fig. S1

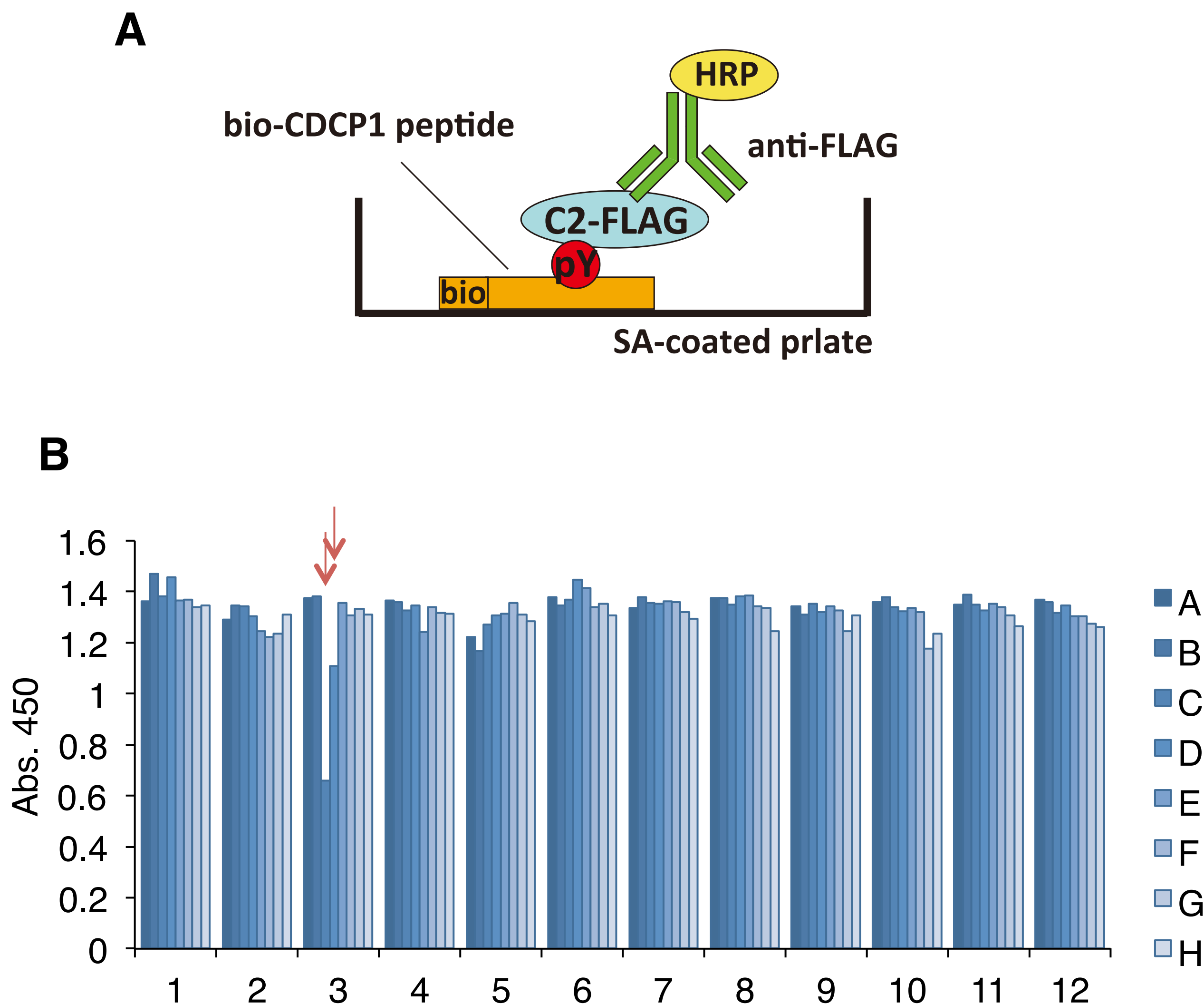
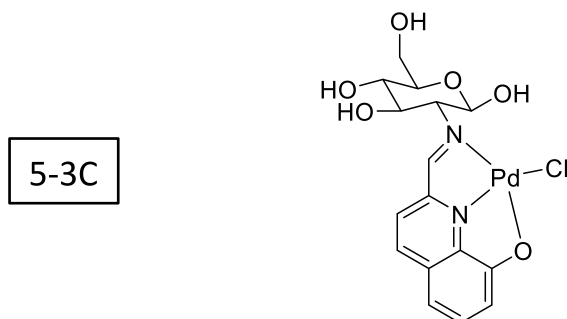


Fig. S1, Chemical Screening

A, Scheme of CDCP1-C2 binding assay. Biotinylated peptide (bio-CDCP1) was immobilized on streptavidin (SA)-coated plate. C2-FLAG recombinant protein was bound to the peptide and then the bound protein was detected by colorimetric reaction of TMB following binding of anti-FLAG antibody conjugated with peroxidase. B, Chemical screening. Chemical screening was performed as described in MATERIALS AND METHODS. The graph shows that the results of a plate that containing positive well, 5-3C and 5-3D (arrows).

Fig. S2

(1) Pd-Oqn = Chloror{N-(hydroxo-quinoline-2-ylmethylidene)-�-D-glucosamine)palladium(II)



Chemical Formula: $C_{16}H_{17}ClN_2O_6Pd$
Molecular Weight: 475.19

Pd-Oqn: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.54 (d, J = 8.8 Hz, 1H), 8.20 (s, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.45 (t, J = 8.4 Hz, 1H), 7.11 (d, J = 6.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.58 (d, J = 8.4 Hz, 1H), 5.53-5.44 (m, 2H), 5.18 (d, J = 4.4 Hz, 1H), 4.58 (t, J = 6.0 Hz, 1H), 4.19 (td, J = 8.8 Hz, 5.6 Hz, 1H), 3.75-3.66 (m, 1H), 3.47-3.37 (m, 1H), 3.31-3.24 (m, 1H), 3.13 (td, J = 8.8 Hz, J = 4.4 Hz, 1H), 2.87 (t, J = 8.8 Hz, 1H).

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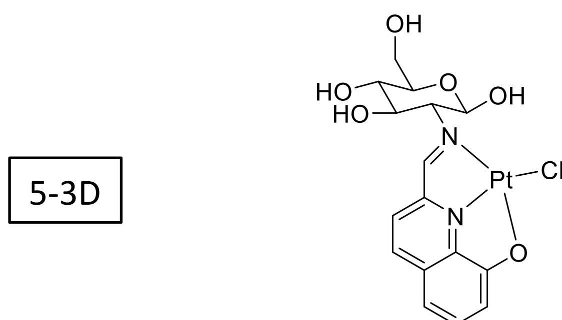
(2) Pt-Oqn = Chloror{N-(hydroxo-quinoline-2-ylmethylidene)-�-D-glucosamine)platinum(II)



Chemical Formula: $C_{16}H_{17}ClN_2O_6Pt$
Molecular Weight: 563.854

Pt-Oqn: ^{1}H NMR (400 MHz, DMF-d_7) δ 8.57 (s, 1H), 8.53 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 6.4 Hz), 6.99 (d, J = 7.6 Hz, 1H), 6.61 (d, J = 7.6 Hz, 1H), 5.82 (t, J = 7.2 Hz, 1H), 5.71 (d, J = 5.2 Hz, 1H), 5.31 (d, J = 5.2 Hz, 1H), 4.75 (t, J = 6.0 Hz, 1H), 4.58 (td, J = 5.2 Hz, J = 9.2 Hz), 3.93-3.85 (m, 1H), 3.68-3.60 (m, 1H), 3.57-3.49 (m, 2H), 3.39-3.26 (m, 2H).

Fig. S2, Structures of the inhibitory compounds for the C2-CDCP1 interaction

Fig. S3

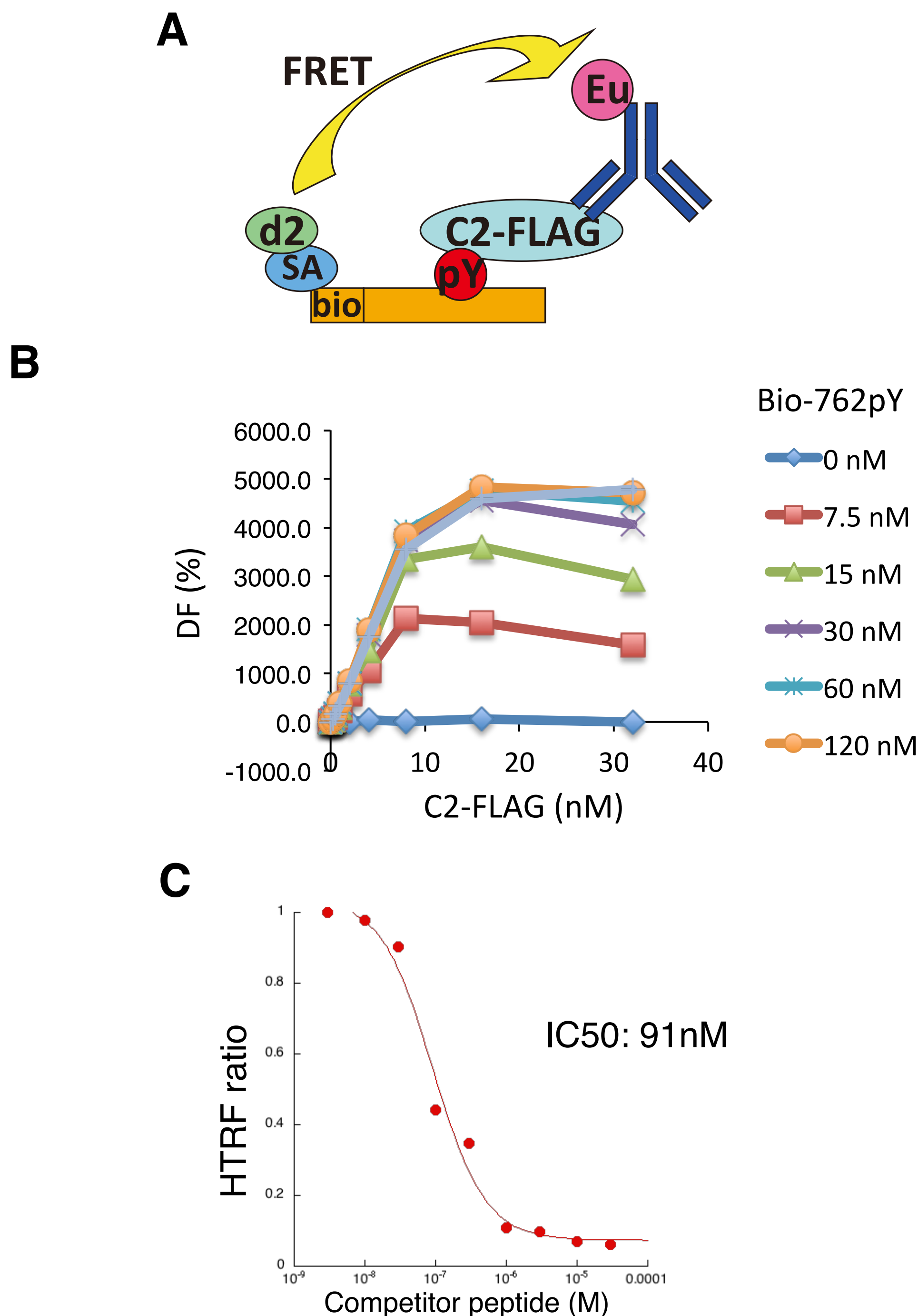


Fig. S3. HTRF assay

A, Scheme of HTRF assay for CDCP1-PKCdelta binding. Homogeneous time-resolved fluorescence (HTRF) assay measures the signal generated by two components when they are in close proximity. The C2-CDCP1 binding assay uses a biotinylated peptide (bio-762-pY) derived from the PKCdelta-binding domain of CDCP1 and recombinant C2-FLAG protein. Binding is detected by anti-FLAG-Eu and streptavidin (SA)-d2. Upon binding of bio-762pY and C2-FLAG, Eu and d2 are brought in close proximity resulting in energy transfer between the two fluorophors and a long-lived signal at 665 nm, which represents the bound fraction. B, Dose-dependent signal of HTRF on C2-CDCP1 binding assay. C, Inhibition of C2-CDCP1 binding by free peptide CP762pY.

Fig. S4

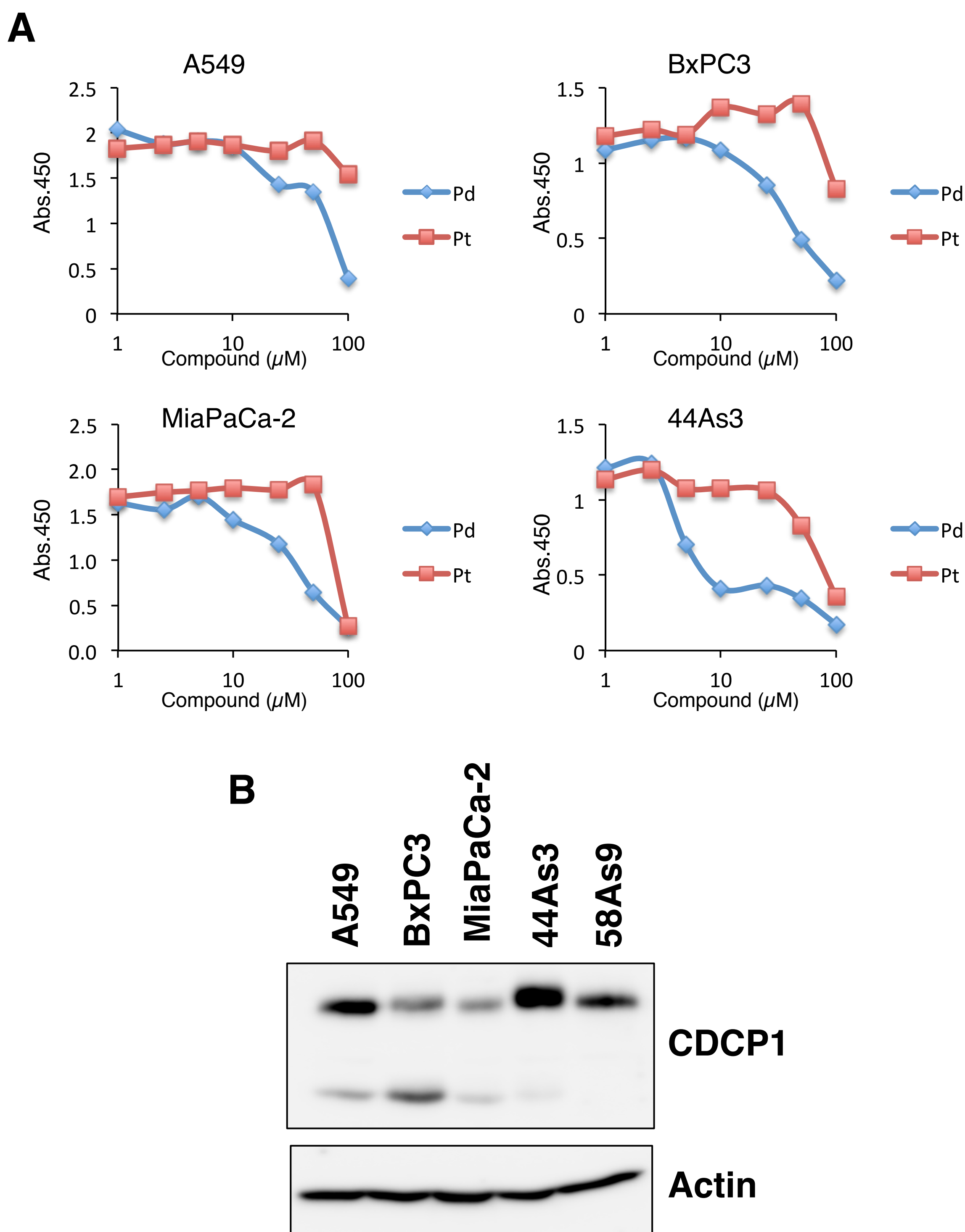


Fig. S4. Effect of the compounds on proliferation of cancer cells

A, Inhibition of the cell proliferation by Pd-Oqn and Pt-Oqn. The cells were seeded on 96-well plate at 3 x 10^3 cells/well with or without these compounds. The cell viability after 48 hrs was measured by CCK assay.

Fig. S5

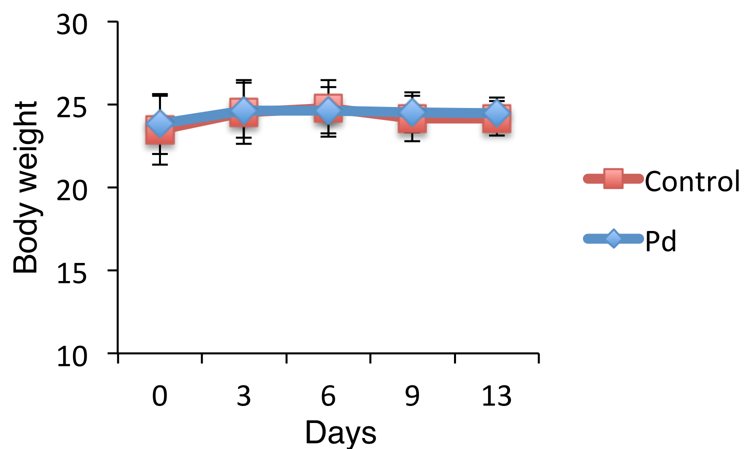


Fig. S5. Body weight of the mice treated with Pd-Oqn
Injection of Pd-Oqn (blue) or DMSO (red) on mouse peritoneal dissemination model was performed as described in Fig. 6A. The graph indicated the body weight as the mean ± standard error (DMSO; n=11, Pd-Oqn; n=13).

Fig. S6

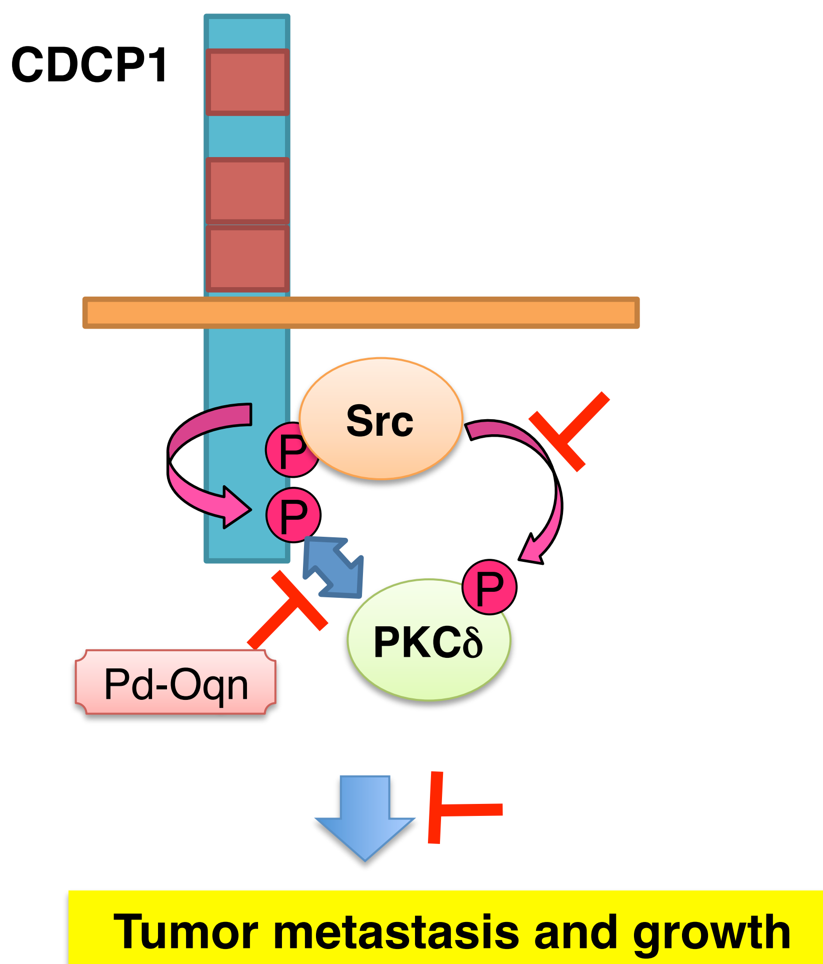


Fig. S6. Model for molecular action of Pd-Oqn
CDCP1 that is a transmembrane protein is predominantly expressed in various cancer cells. Intracellular region of CDCP1 is tyrosine-phosphorylated by Src family kinases. PKCδ is recruited to the phosphorylated site and also phosphorylated by SFK, which plasy important role for anchorage-independent cell growth and cancer metastasis. The small molecule Pd-Oqn identified here inhibits the interaction of PKCδ with phosphorylated CDCP1 and PKCδ is eventually inhibited its phosphorylation The blocking CDCP1-PKCδ pathway results in the suppression of tumor metastasis and growth.

Fig. S7

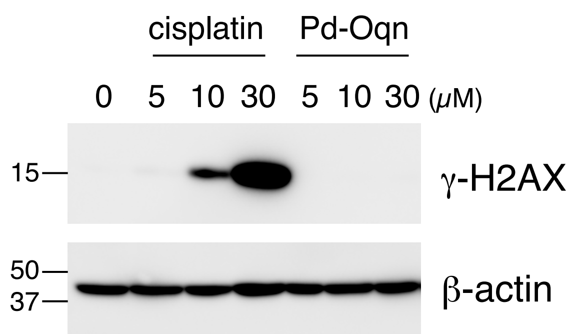


Fig. S7. No DNA damage response by Pd-Oqn
44As3 cells were treated with the indicated concentration of cisplatin or Pd-Oqn for 4hrs and then lysed in RIPA buffer (25mM Tris-HCl (pH 7.4), 150mM NaCl, 1% NP-40, 1% sodium deoxycholate, and 0.1% SDS) containing phosphatase inhibitor and protease inhibitor. The cell lysate was subjected to western blotting with anti-γH2AX or anti-β-actin.