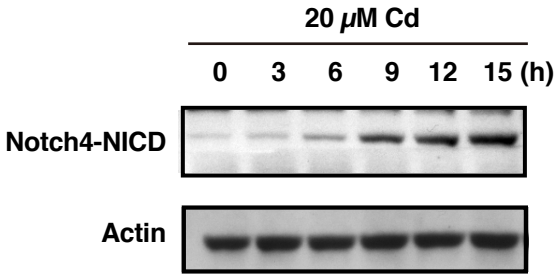
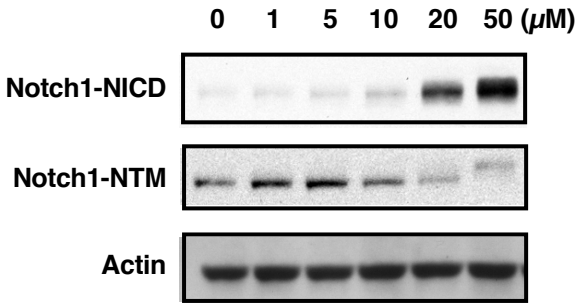
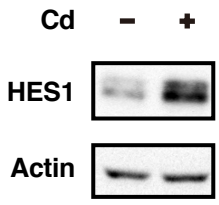


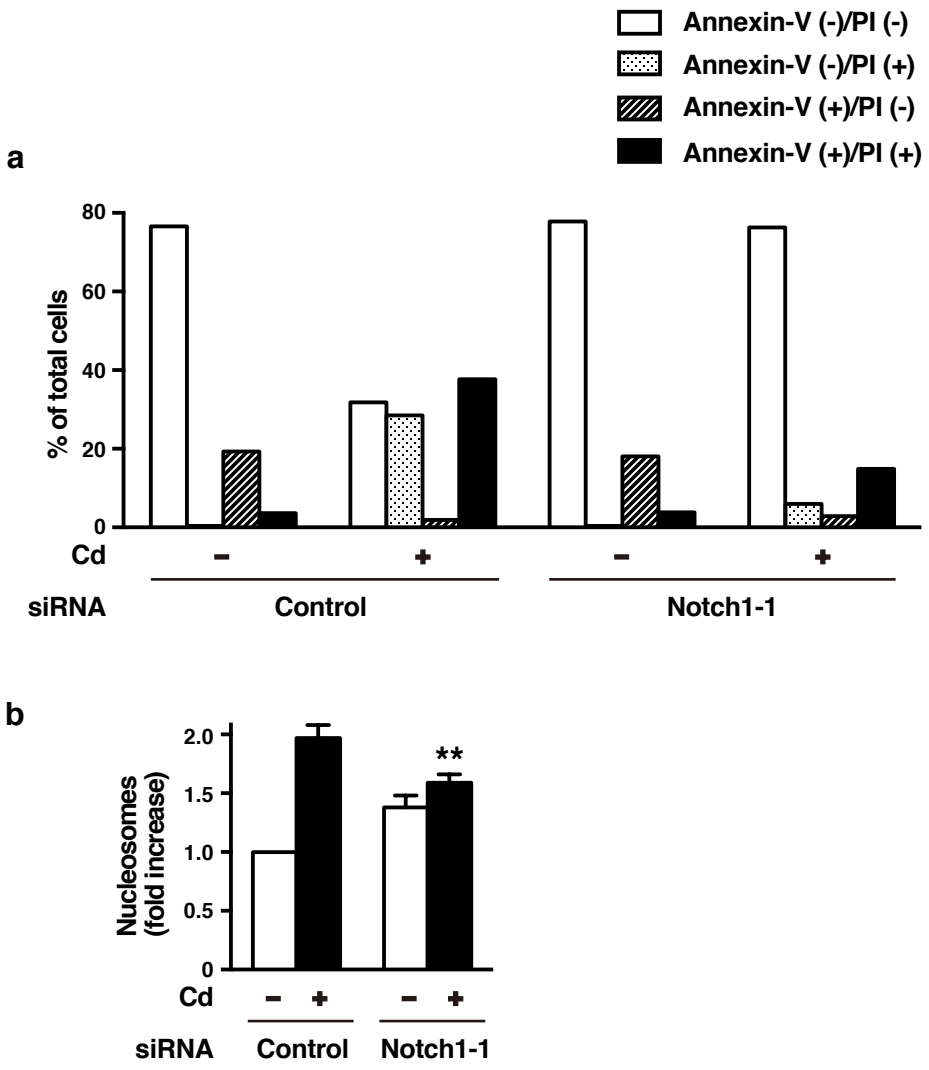
Supplementary Figure 1. Effects of cadmium exposure on the levels of Notch4-NICD in HK-2 cells. Cells were incubated with 20 μM $CdCl_2$ (Cd) for the indicated time. Cell lysates were subjected to western blotting using antibodies against Notch4-NICD and actin. Immunoblots shown are representative of at least three independent experiments



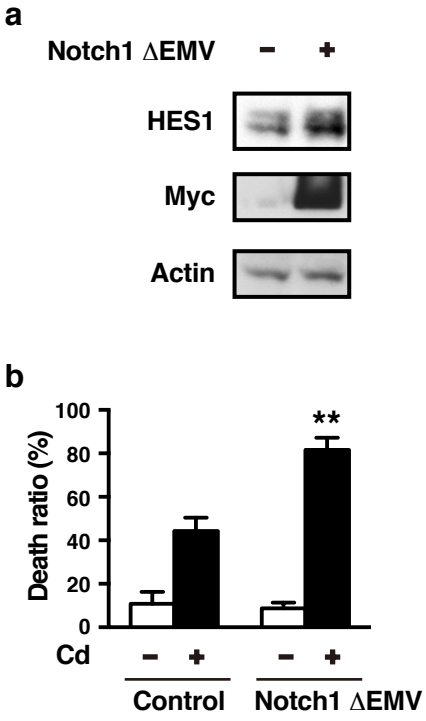
Supplementary Figure 2. Dose effects of cadmium exposure on the levels of Notch1-NICD in HK-2 cells. Cells were incubated with 1, 5, 10, 20, or 50 μM $CdCl_2$ for 12 h. Cell lysates were subjected to western blotting using antibodies against Notch1-NICD, Notch1-NTM, and actin. Immunoblots shown are representative of at least three independent experiments



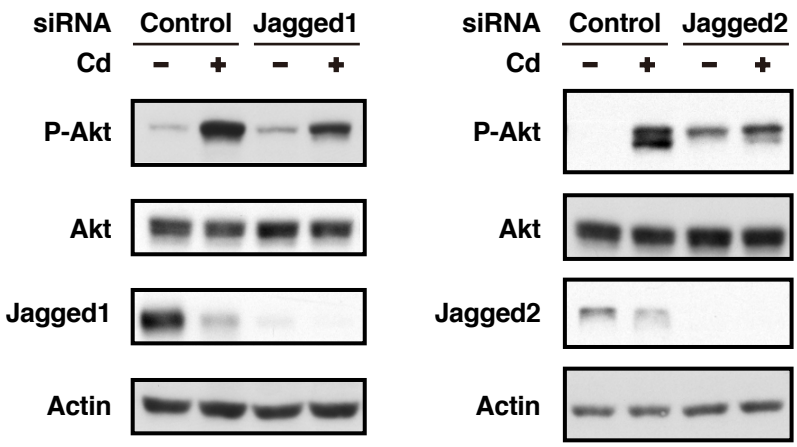
Supplementary Figure 3. Expression of Hes1 in HK-2 cells exposed to $CdCl_2$. Cells were incubated with or without 20 μM $CdCl_2$ (Cd) for 3 h. Cell lysates were subjected to western blotting using antibodies against HES1 and actin. Immunoblots shown are representative of at least three independent experiments.



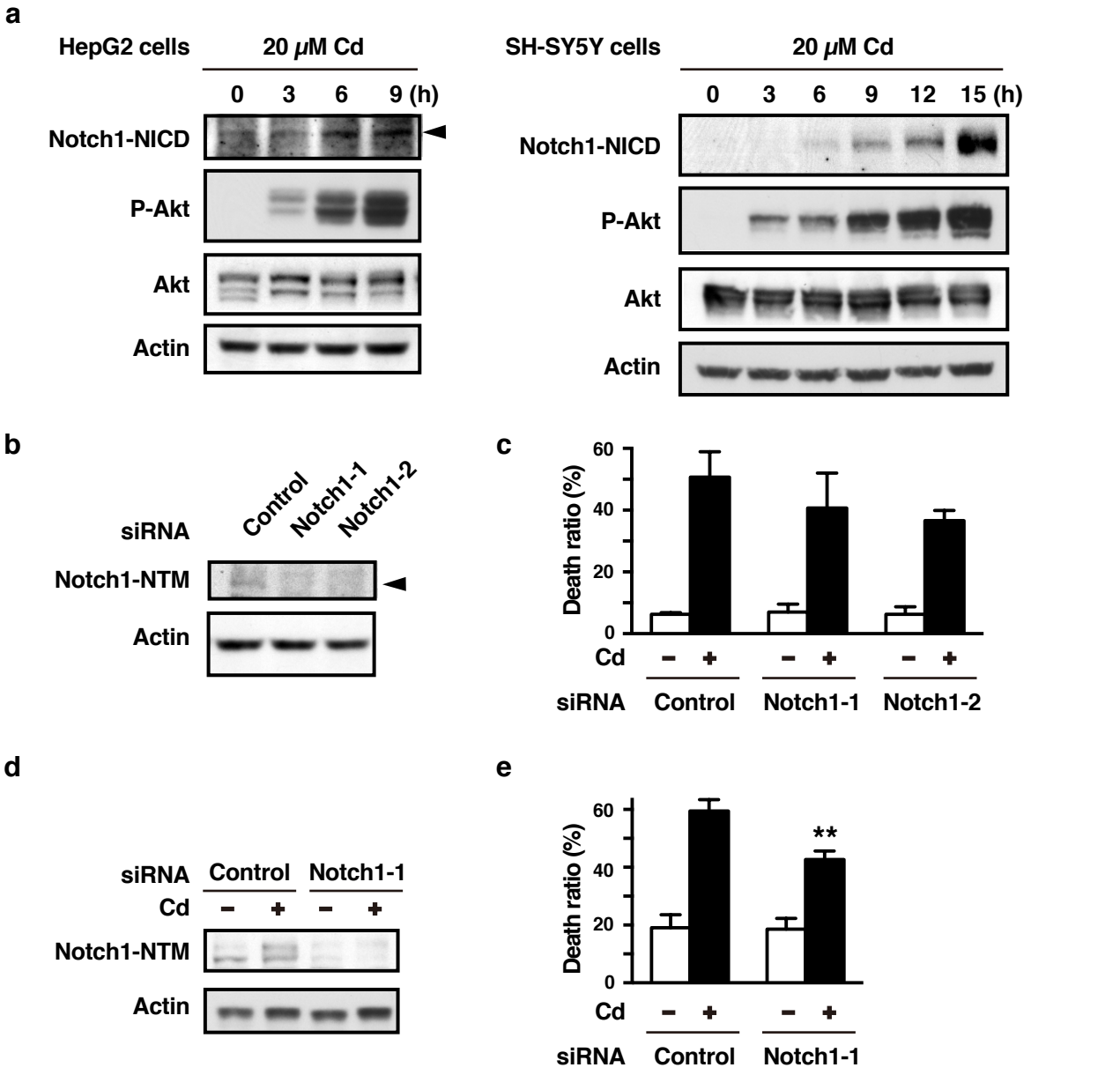
Supplementary Figure 4. Involvement of Notch1 signaling in $CdCl_2$-induced apoptotic cell death in HK-2 cells. (a) Cells transfected with control siRNA or Notch1 siRNA-1 were incubated with or without 25 μM $CdCl_2$ (Cd) for 30 h. Percentage of live, necrotic (propidium iodide [PI] positive), early apoptotic (Annexin-V positive), and late apoptotic cells (Annexin-V/PI double positive) was determined by Annexin-V and PI staining. Results are representative of at least three independent experiments. (b) Cells transfected with control siRNA or Notch1 siRNA-1 were incubated with or without 20 μM $CdCl_2$ (Cd) for 16 h. The cytoplasmic fraction was used in an enzyme-linked immunosorbent assay to measure the levels of nucleosomes. Each values is the fold increase with respect to the untreated control (control siRNA without Cd) and reflects the mean ± SD of three experiments with triplicate assays in each experiment. $^{**}P < 0.01$ vs. $CdCl_2$-treated cells transfected with control siRNA.



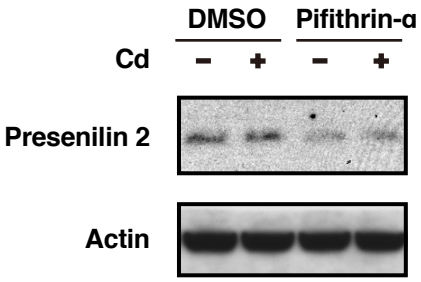
Supplementary Figure 5. Effects of hyperactivation of Notch1 signaling on $CdCl_2$-induced cellular damage in HEK293T cells. (a) Cells were transfected with or without Notch1 ΔEMV plasmid for 24 h. Cell lysates were subjected to western blotting using antibodies against HES1, Myc, and actin. Immunoblots shown are representative of at least three independent experiments. (b) Cells transfected with or without Notch1 ΔEMV plasmid were incubated with or without 25 μM $CdCl_2$ (Cd) for 30 h. The viability of cells was determined by trypan blue exclusion assay. Each value is the percentage of trypan blue-positive cells and reflects the mean ± SD of three experiments with duplicate assays in each experiment. $^{**}P < 0.01$ vs. $CdCl_2$-treated cells without Notch1 ΔEMV transfection.



Supplementary Figure 6. Effects of knockdown of Jagged1 or Jagged2 expression on $CdCl_2$-induced phosphorylation of Akt in HK-2 cells. Cells transfected with control siRNA, Jagged1 siRNA, or Jagged2 siRNA were incubated with or without 20 μM $CdCl_2$ (Cd) for 12 h. Cell lysates were subjected to western blotting using antibodies against phospho-Akt, total Akt, Jagged1 (left), Jagged2 (right), and actin. Immunoblots shown are representative of at least three independent experiments.



Supplementary Figure 7. Effects of Notch1 signaling on $CdCl_2$-induced cellular damage in HepG2 and SH-SY5Y cells. (a) HepG2 cells (left) and SH-SY5Y cells (right) were incubated with 20 μM $CdCl_2$ (Cd) for the indicated time. The untreated control is labeled 0 h. Cell lysates were subjected to western blotting using antibodies against Notch1-NICD, phospho-Akt, total Akt, and actin. (b, c) HepG2 cells transfected with control siRNA, Notch1 siRNA-1, or Notch siRNA-2 were incubated with or without 20 μM $CdCl_2$ (Cd) for 12 h (b) or 30 h (c). Cell lysates were subjected to western blotting using antibodies against Notch1-NTM and actin (b). The viability of cells was determined by trypan blue exclusion assay. Each value is the percentage of trypan blue-positive cells and reflects the mean ± SD of three experiments with duplicate assays in each experiment (c). (d, e) SH-SY5Y cells transfected with control siRNA or Notch1 siRNA-1 were incubated with or without 20 μM $CdCl_2$ (Cd) for 9 h (d) or 18 h (e). Cell lysates were subjected to western blotting using antibodies against Notch1-NTM and actin (d). The viability of cells was determined by trypan blue exclusion assay. Each value is the percentage of trypan blue-positive cells and reflects the mean ± SD of four experiments with duplicate assays in each experiment. $^{**}P < 0.01$ vs. $CdCl_2$-treated cells transfected with control siRNA (e). Immunoblots shown are representative of at least three independent experiments



Supplementary Figure 8. Effects of p53 inhibitor pifithrin-α on presenilin 2 expression in HK-2 cells. Cells were incubated with 0.1% DMSO or 40 μM pifithrin-α for 1 h and then incubated with or without 20 μM $CdCl_2$ (Cd) for 9 h. Cell lysates were subjected to western blotting using antibodies against presenilin2 and actin. The presenilin2 antibody detects the carboxy-terminal fragment of presenilin 2. Immunoblots shown are representative of at least three independent experiments.