Figure S1. CYLD expression following AZA treatment. Representative western blot of CYLD protein expression following 72 h treatment with AZA (5 μM) relative to β-actin. CYLD, CYLD lysine 63 deubiquitinase; AZA, 5-Aza-deoxycytidine; Ctrl, control.

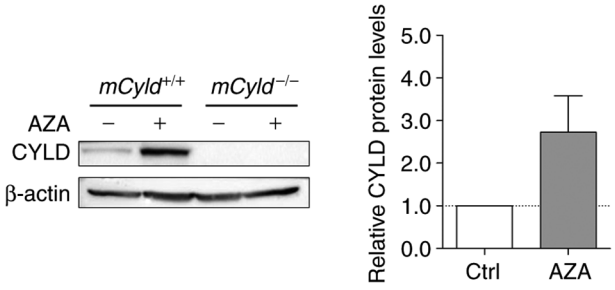

Figure S2. CYLD protein expression following inhibitor treatment. Representative western blot of CYLD protein expression (relative to β-actin) following 24 h treatment with Chaetocin in (A) murine and (B) h and JIB04 in (C) murine and (D) h cells. CYLD, CYLD lysine 63 deubiquitinase; JIB04, Jumonji histone demethylase inhibitor; Ctrl, control; h, human; m, mouse.

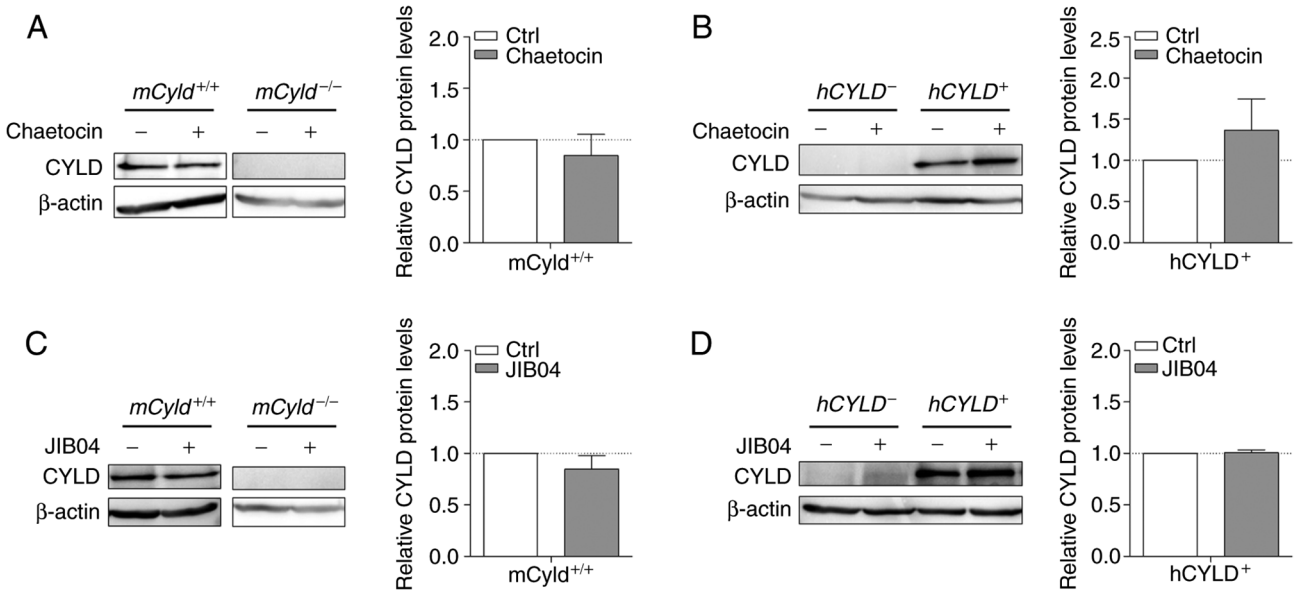

Figure S3. Role of the deubiquitinase function of CYLD. Effect of CM272 treatment on catalytically inactive *CYLD* melanoma cells (*hCYLD*$^{C/S}$). (A) Representative western blot of H3K9me2 levels following 24 h treatment with CM272 (200 nM) relative to H3. (B) Representative images of anchorage-dependent clonogenic assay. (C) Representative western blot of CYLD protein expression following 24 h treatment with CM272 relative to β-actin. (D) Chromatin accessibility assay of *hCYLD*$^{+}$ and *hCYLD*$^{C/S}$ relative to *hCYLD*$^{-}$ cells. (E) Representative western blot analysis of EHMT2 protein expression in *hCYLD*$^{C/S}$ and h*CYLD*$^{-}$ cells (relative to β-actin). (F) Validation of H3K9me2 levels in *hCYLD*$^{C/S}$ and h*CYLD*$^{-}$ cells. *P<0.05. ns, not significant; EHMT2, euchromatic histone lysine methyltransferase 2; CYLD, CYLD lysine 63 deubiquitinase; Ctrl, control; h, human; H3, histone 3.