



**Extended Data Figure 8 | Depletion of *Cdh1*, but not *Cdc20*, prolongs SPOP proteins stability, which is simultaneously coupled with a decrease in PD-L1 protein level. a-c**, Immunoblot (IB) analysis of whole cell lysates (WCL) derived from HeLa depleted *SPOP* through the CRISPR-Cas9 system (a) or depleted *Cdc20* or *Cdh1* through multiple independent shRNAs (b, c). **d**, IB analysis of WCL and immunoprecipitation (IP) derived from 293T cells transfected with indicated constructs and treated with MG132 (10  $\mu$ M) for 12 hours before harvesting. **e**, IB analysis of WCL and IP derived from HeLa cells treated with MG132 (10  $\mu$ M) for 12 hours

before harvesting. **f**, A sequence comparison of D-box motif (RxxLxxxxN) in SPOP derived from different species. **g**, IB analysis of WCL derived from HeLa cells transfected with indicated constructs. **h**, **i**, IB analysis of WCL derived from 293T cells transfected with indicated constructs. 36 h post transfection, cells were treated with cycloheximide (CHX) as indicated time points before harvesting (**h**). The protein abundance of SPOP-WT and deletion of RxxL mutant were quantified by the ImageJ software (**i**).