Extended Data Figure 6 | Cancer-derived SPOP mutations fail to promote PD-L1 degradation. a, The mutation frequency (mutated cases/total cases) of SPOP across 24 cancer types from the TCGA database. Mutations are categorized as happening in the MATH domain, in the BTB domain or at any other position of the gene, including UTRs. Because some patient cases contain mutations of two or three categories, the proportion of three colors are allocated mutation-wise, instead of case-wise. **b,** The distribution of mutation positions of SPOP in 24 cancer types from the TCGA database. Mutations with low translational consequences have been discarded. **c,** Immunoblot (IB) analysis of whole cell lysates (WCL) derived from 293T cells transfected with indicated constructs. **d,** The mutation frequency (mutated cases/total cases) of PD-L1 (CD274) across 19 cancer types from the TCGA database. **e,** Oncoplot of PD-L1 (CD274) and SPOP across all 39 cancer types in the TCGA database. Only mutations or truncations in the C terminal tail of PD-L1 or in the MATH domain of SPOP are counted. **f,** IB of WCL derived from B16-F10 mouse tumor cell line stably expressing the indicated SPOP constructs. **g, h,** Growth curve and cell cycle profile of B16-F10 cells stably expressing SPOP WT and the F102C mutant as well as EV as a negative control. **i,** Cell cycle profile of 22Rv1 cells stably expressing SPOP WT and the F102C mutant as well as EV as a negative control. **j,** Relative cell surface PD-L1 expression of 4T1 implanted tumors ectopically expressing SPOP-WT or the SPOP-F102C mutant were subjected to FACS analysis. n = 5 mice per experimental group. **k,** B16-F10 cells stably expressing SPOP-WT or the SPOP-F102C mutant implanted tumors from C57BL/6 mice were dissected and taken a picture after euthanizing the mice. **l,** The number of $CD3^+$ T-cell populations from the isolated tumor-infiltrating lymphocytes in 4T1 cells stably expressing SPOP-WT or the SPOP-F102C mutants implanted tumors were subjected to FACS analysis. n = 5 mice per experimental group. **m,** B16-F10 cells stably expressing SPOP-WT or the SPOP-F102C mutant implanted tumors from C57BL/6 mice treated with anti-PD-L1 antibody were dissected and taken a picture after euthanizing the mice. n = 7 mice per experimental group. **n,** The weight of B16-F10 cells implanted tumors from C57BL/6 mice treated with anti-PD-L1 antibody. 12 mice per experimental group. **o,** Relative cell surface PD-L1 expression of B16-F10 cells implanted tumors ectopically expressing SPOP-WT or the SPOP-F102C mutant treated with anti-PD-L1 antibody were subjected to FACS analysis. n = 5 mice per experimental group. **p,** The number of $CD3^+$ T-cell populations from the isolated tumor-infiltrating lymphocytes in B16-F10 cells implanted tumors ectopically expressing SPOP-WT or the SPOP-F102C mutant treated with control IgG or anti-PD-L1 antibody were subjected to FACS analysis. n = 7 mice per experimental group. **q,** B16-F10 cells stably expressing SPOP-WT or the SPOP-F102C mutant implanted tumors from $Tcr\alpha^{-/-}$ mice were dissected and taken a picture after euthanizing the mice. n = 7 mice per experimental group. **r,** Relative cell surface PD-L1 expression of B16-F10 cells stably ectopically expressing SPOP-WT or the SPOP-F102C mutant implanted tumors from $Tcr\alpha^{-/-}$ mice were subjected to FACS analysis. n = 7 mice per experimental group. **s,** The number of $CD3^+$ T-cell populations from the isolated tumor-infiltrating lymphocytes in B16-F10 cells stably ectopically expressing SPOP-WT or the SPOP-F102C mutant implanted tumors from $Tcr\alpha^{-/-}$ mice were subjected to FACS analysis. n = 7 mice per experimental group. Error bars, ± s.d., two-tailed *t*-test, $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, NS: no significance.