

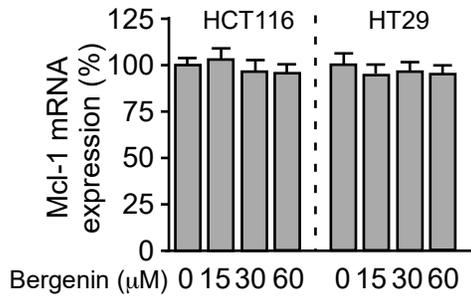
**Supplementary Figure S1** A, HCT116 and HT29 cells were treated with bergenin for 48 h, the mRNA level of Mcl-1 was examined by qRT-PCR. B, HCT116 cells were co-transfected with Flag-Mcl-1 and His-ubiquitin K-only mutant series (K6, K11, K27, K29, K33, K48, K63, WT) for 24 h, incubated with bergenin for 48 h, followed by culture with 20  $\mu$ M MG132 for 6 h. Ni-NTA pull-down assay was performed to detect Mcl-1 ubiquitination. C, HCT116 cells were incubated with bergenin for 48 h, followed by culture with 20  $\mu$ M MG132 for 6 h. Mcl-1 ubiquitination was analyzed with the Ub-K48 specific antibody.

**Supplementary Figure S2.** A. The expression levels of various E3-ligases such as  $\beta$ -TCRP、FBW7、TRIM17、FBXO4、CDC20 and Mule mRNA in tumor tissues (COAD and READ) (red box) and non-tumor tissues (grey box) were analyzed by GEPIA (<http://gepia.cancer-pku.cn/>). \*P<0.05. B. Association between FBW7 (left)、 $\beta$ -TCRP (middle) or TRIM17 (right) protein level and overall survival (OS) of CRC patients assessed by Kaplan–Meier survival curves from Proteinatlas database (<https://www.proteinatlas.org/>).

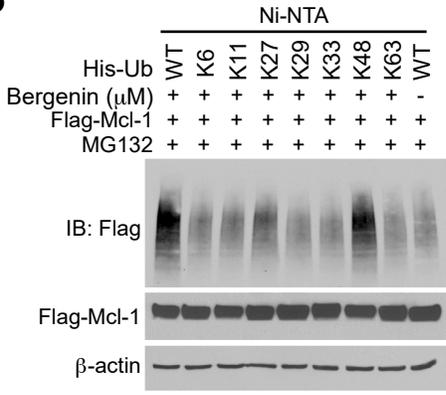
**Supplementary Figure S3.** HE staining of the heart, liver, spleen, lung, and kidney from the vehicle or Bergenin treated mice. Scale bar, 25 $\mu$ m.

# Supplementary Figure S1

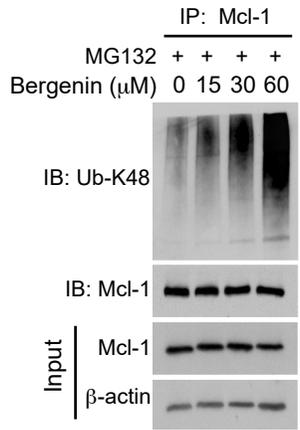
**A**



**B**

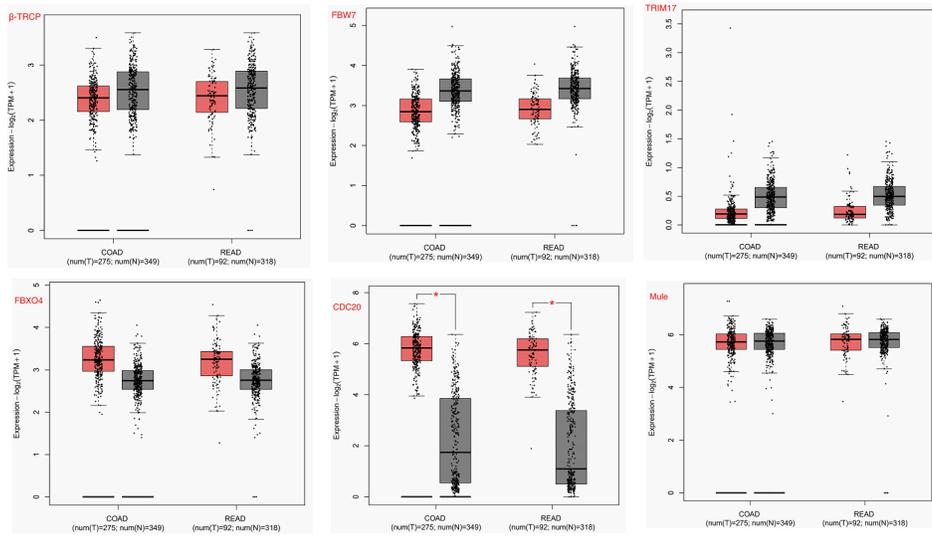


**C**

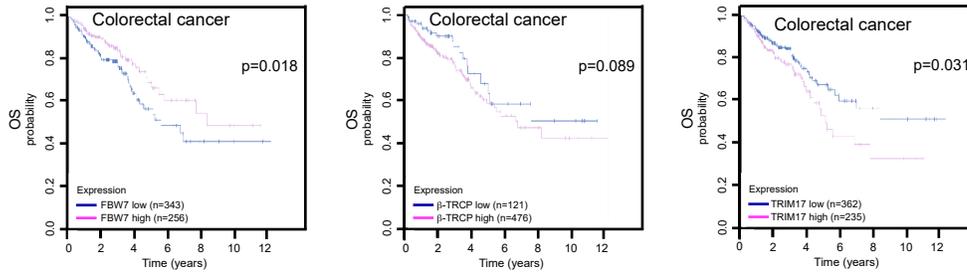


# Supplementary Figure S2

## A

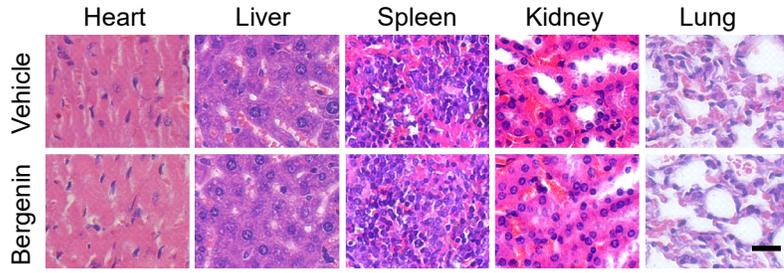


## B

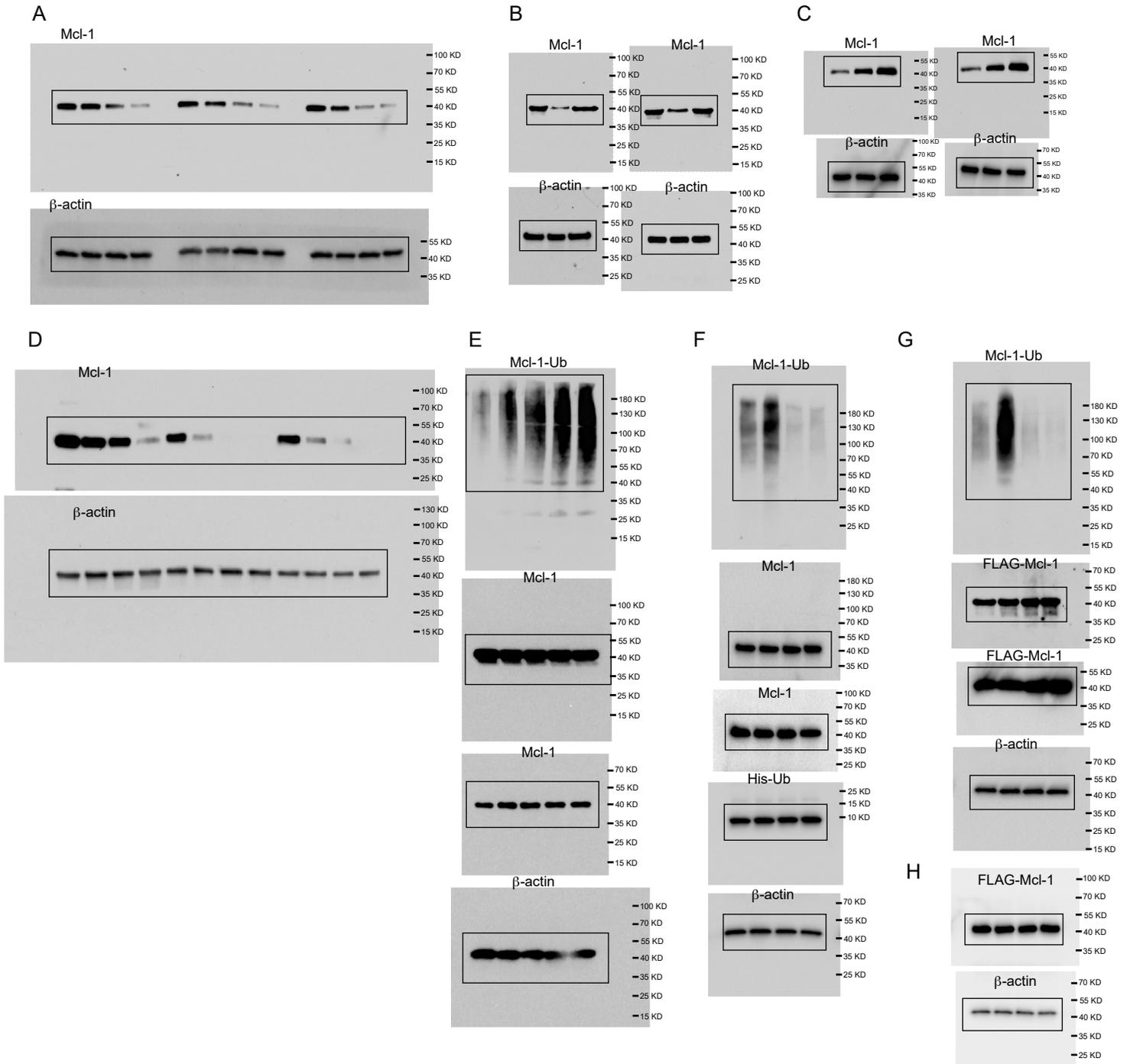


# Supplementary Figure S3

A

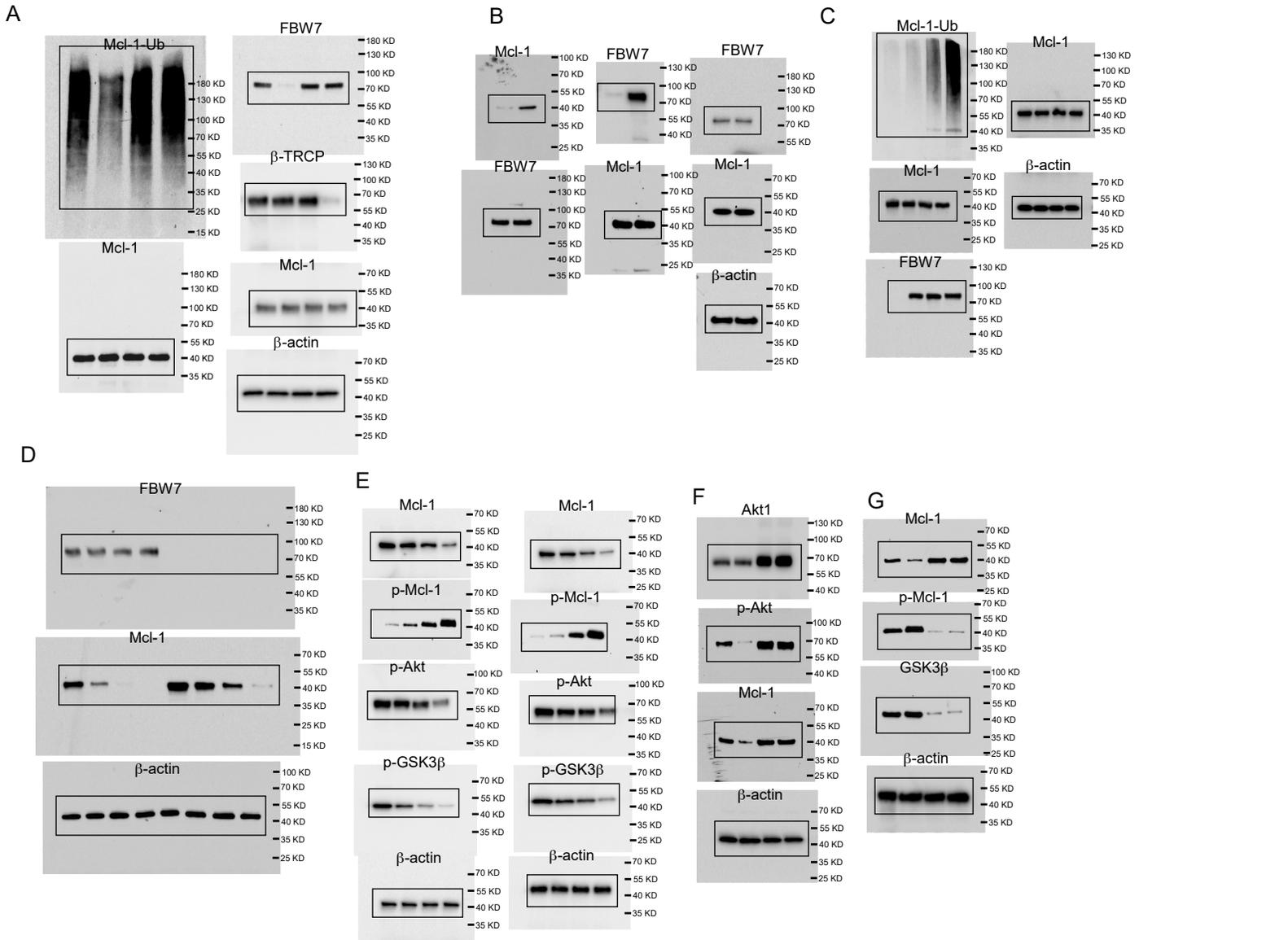


4-1 full gel for Figure 2

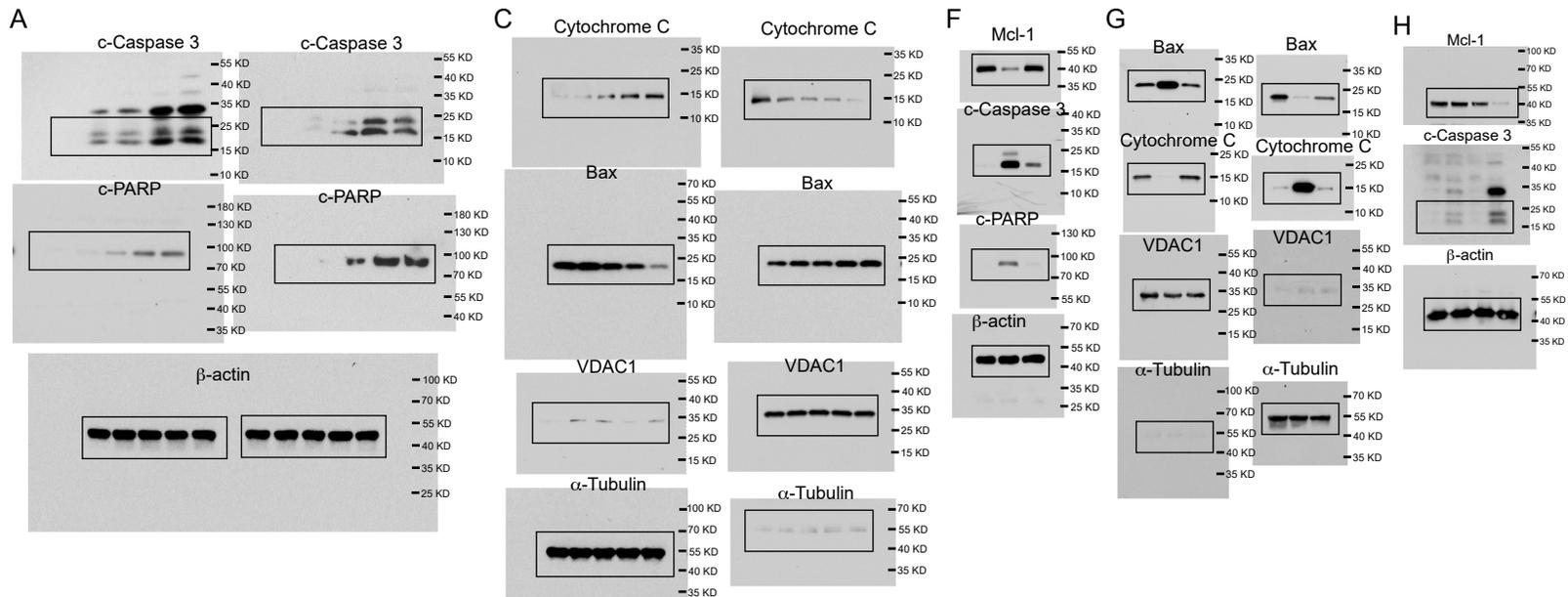


Supplementary Figure S4

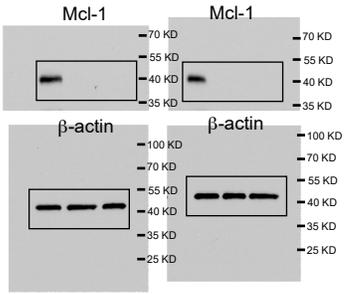
4-2. full gel for Figure 3



4-3. full gel for Figure 4



4-4. full gel for Figure 5B



4-5. full gel for Supplementary Figure S1

