

## **Supplementary Figure legends**

**Supplementary Figure 1. Tubastatin-A enhances CFZ-induced cytotoxicity.** MM.1S (left) and RPMI8226 (right) cells were cultured with indicated concentration of CFZ in the presence of Tubastatin-A (1- 10  $\mu$ M) for 48h. Cell toxicity was assessed by MTT assay, and data represent mean  $\pm$  SD from average of 3 independent experiments. Combination index (CI) was calculated by CalcuSyn software program.

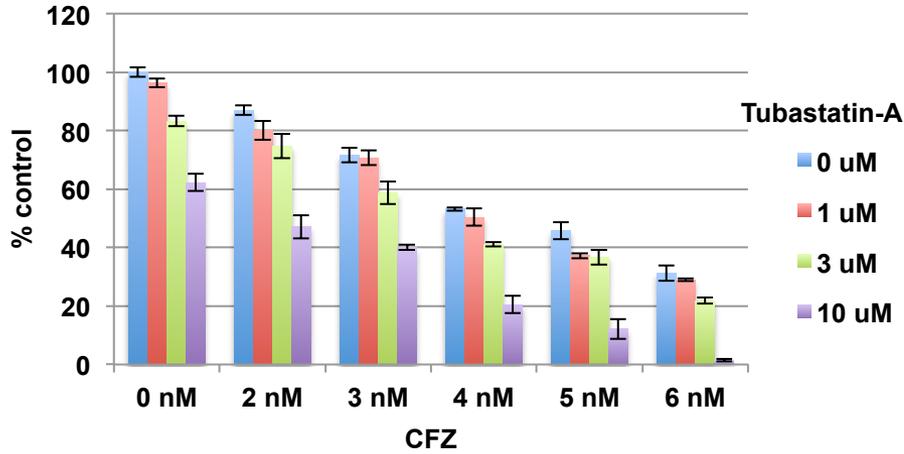
**Supplementary Figure 2. MS275 enhances CFZ-induced cytotoxicity in MM.1S and RPMI8226 cells.** MM.1S (left) and RPMI8226 (right) cells were cultured with indicated concentration of CFZ in the presence of MS275 (1- 10  $\mu$ M) for 48h. Cell toxicity was assessed by MTT assay, and data represent mean  $\pm$  SD from average of 3 independent experiments. Combination index (CI) was calculated by CalcuSyn software program.

**Supplementary Figure 3. Equivalent cytotoxicity induced by CFZ in combination with ACY-1215 or MS275.** RPMI8226 cells were cultured with ACY-1215 (2  $\mu$ M) or MS275 (2  $\mu$ M) in the absence or presence of CFZ (10 nM) for 16h. Cell toxicity was assessed by MTT assay, and data represents mean  $\pm$  SD from average of 3 independent experiments.

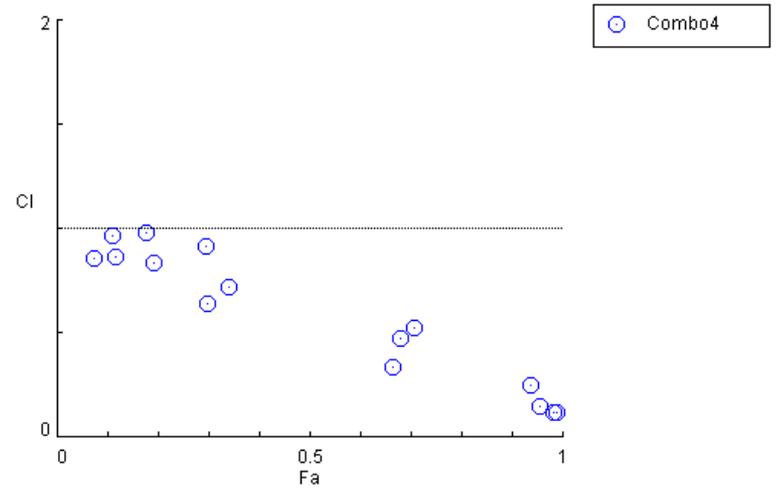
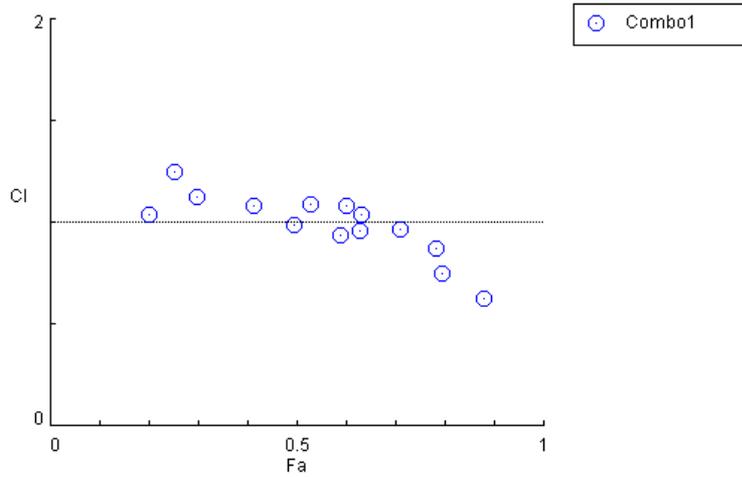
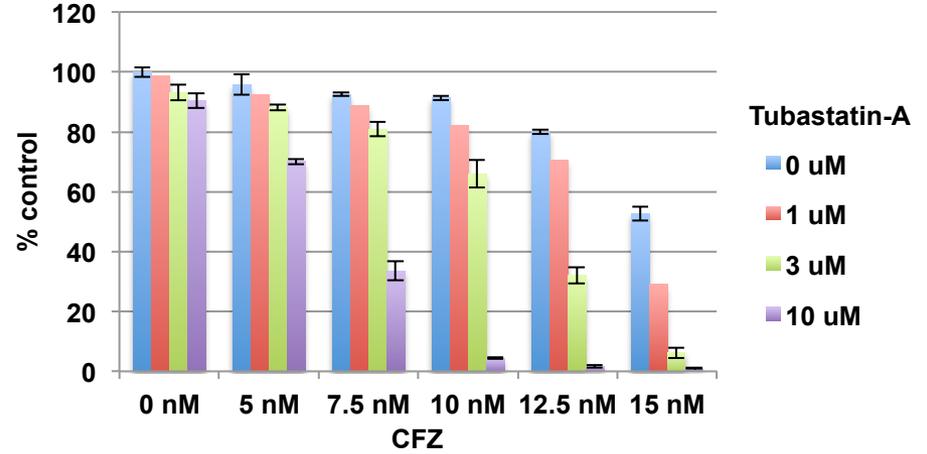
**Supplementary Figure 4. Tunicamycin inhibits MM cell growth.** MM cell lines were cultured with tunicamycin (0.03 – 3  $\mu$ g/ml) for 24h. Cell toxicity was assessed by MTT assay, and data represent mean  $\pm$  SD from average of 3 independent experiments.

**Supplementary Figure 5. Inhibitors of caspases rescue cytotoxicity induced by CFZ in combination with ACY-1215 or MS275.** (A) Primary MM tumor cells were treated with control media, ACY-1215 (2  $\mu$ M) with CFZ, or MS275 (2  $\mu$ M) with CFZ for 16h. Cell lysates were subjected to Immunoblotting with indicated Abs; CF, cleaved fragment. RPMI8226 cells (B) and primary MM tumor cells (C and D) were cultured with control media, ACY-1215 (2  $\mu$ M) with CFZ, or MS275 (2  $\mu$ M) with CFZ in the absence or presence of inhibitors of caspase-8 (Casp-8i, 10  $\mu$ M), caspase-9 (Casp-9i, 10  $\mu$ M) or caspase-10 (Casp-10i, 10  $\mu$ M) for 16h. Cell toxicity was assessed by MTT assay, and data represent mean  $\pm$  SD from triplicated cultures.

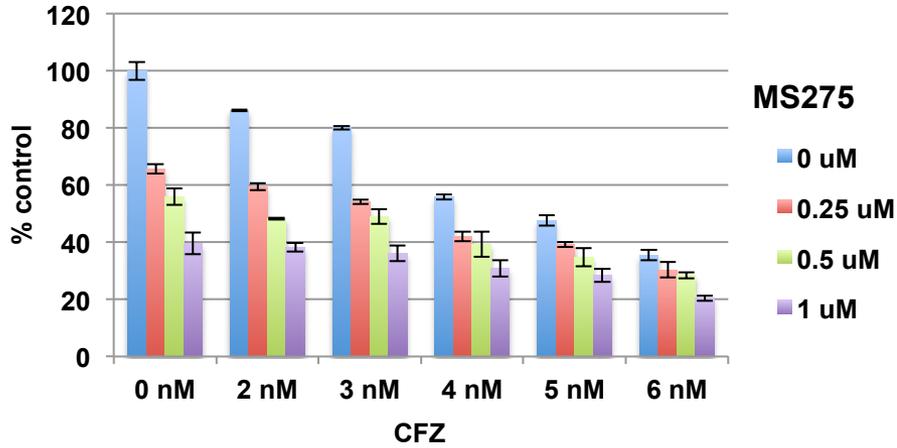
**MM.1S+CFZ+Tubastatin-A (48h MTT)**



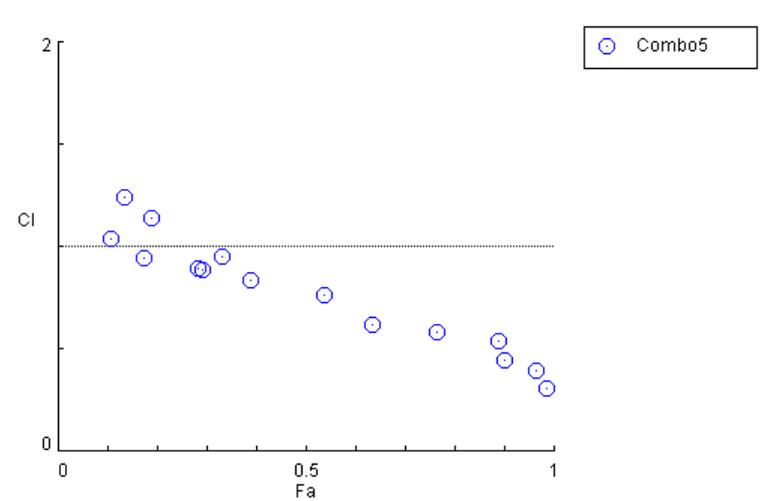
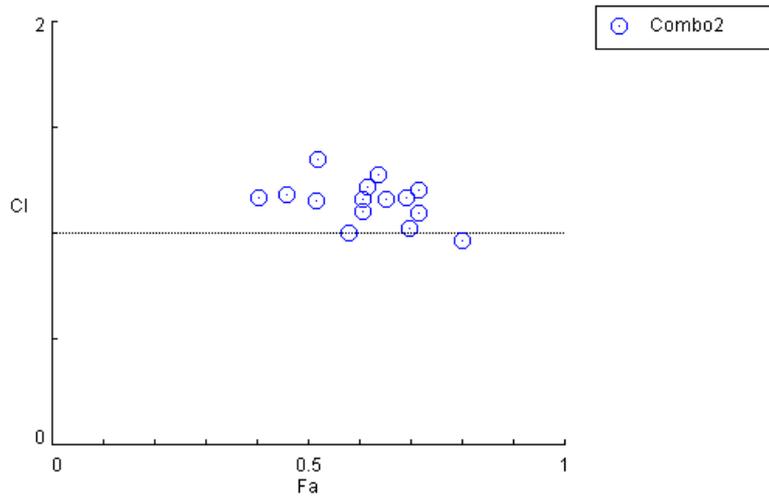
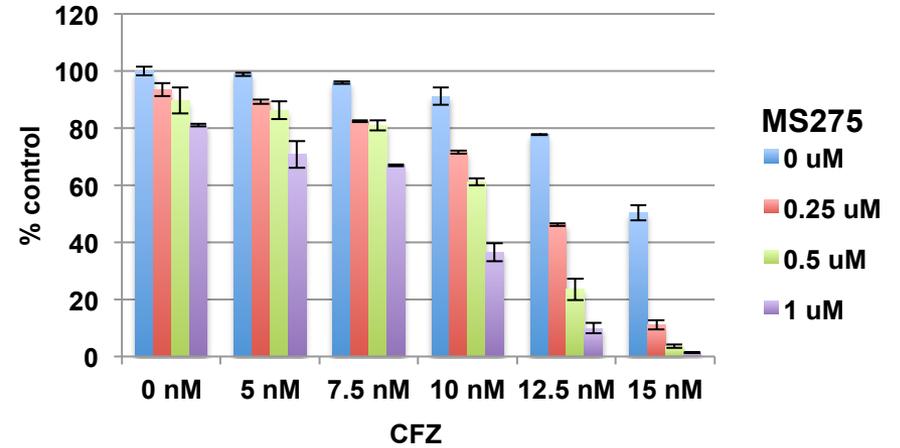
**RPMI8226+CFZ+Tubastatin-A (48h MTT)**

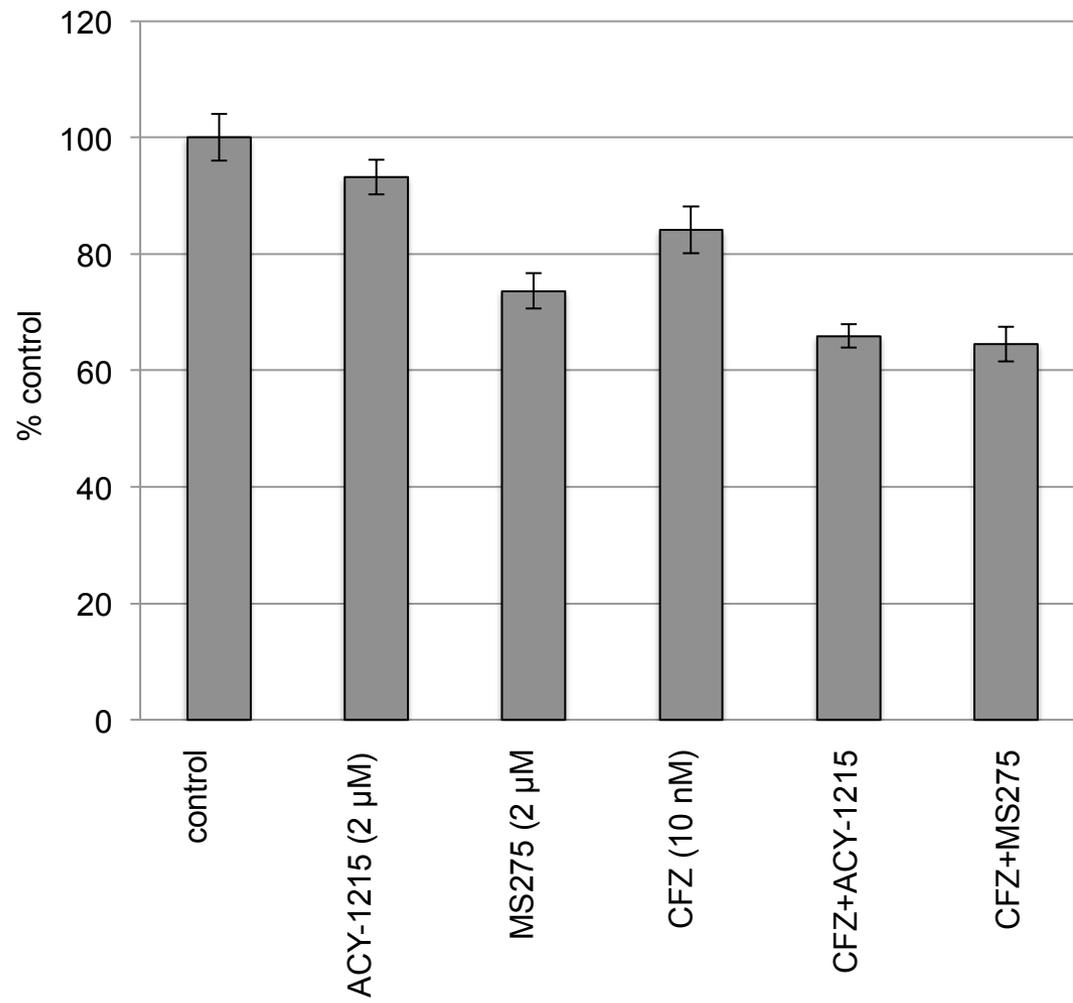


MM.1S+CFZ+MS275 (48h MTT)

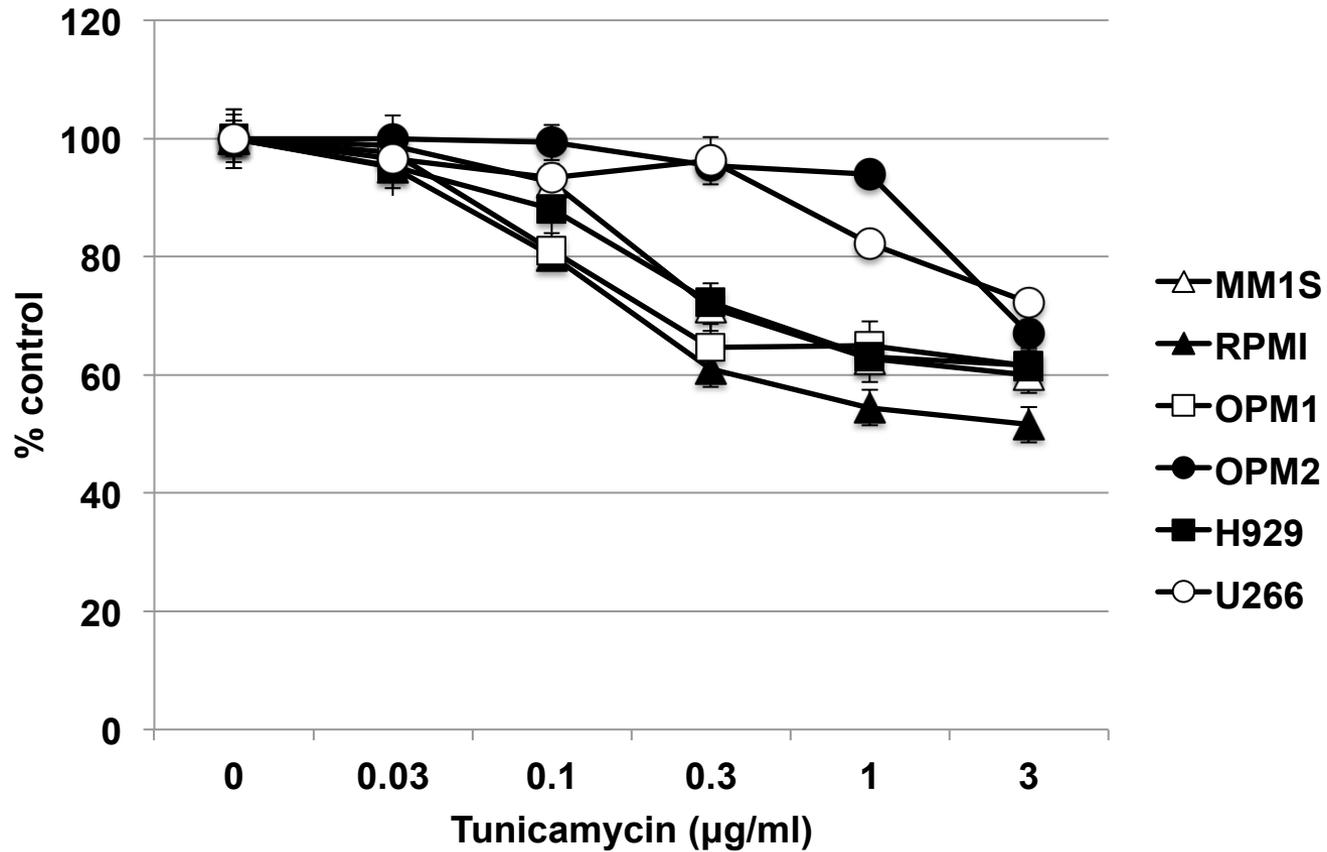


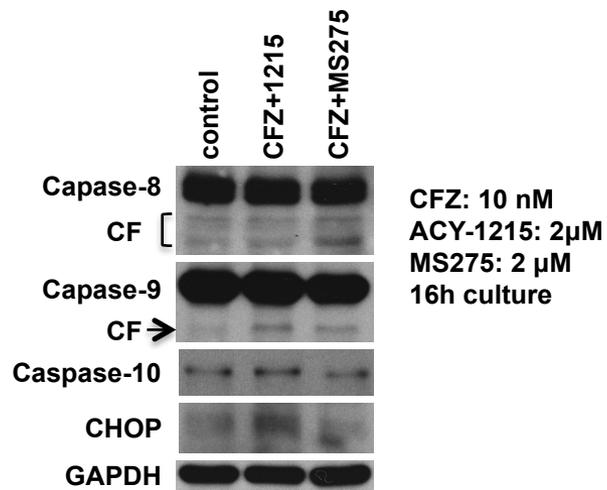
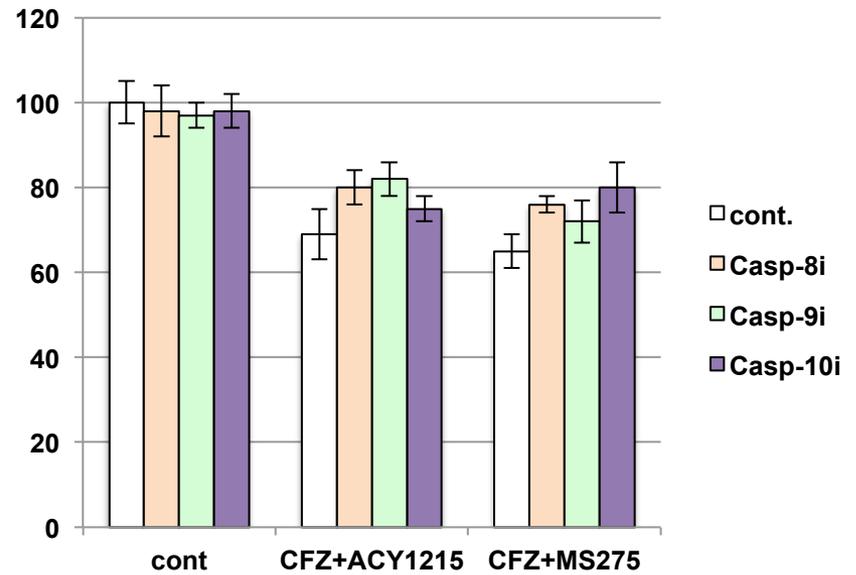
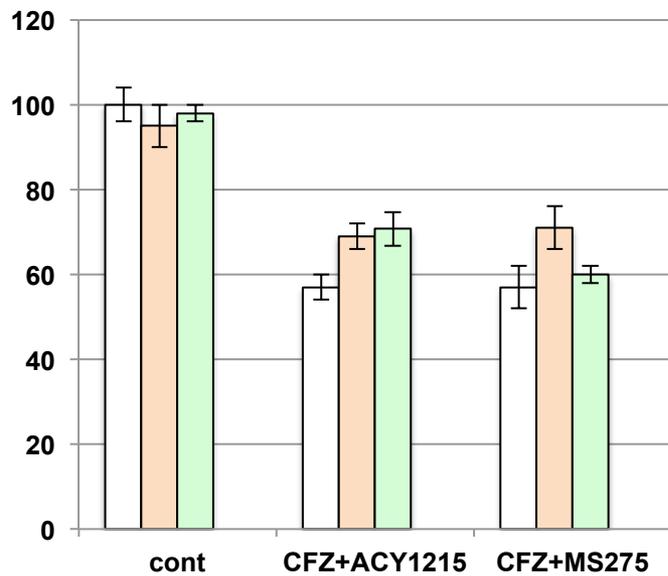
RPMI8226+CFZ+MS275 (48h MTT)





### MM cell lines + Tunicamycin (24h MTT)



**A****B****C****D**