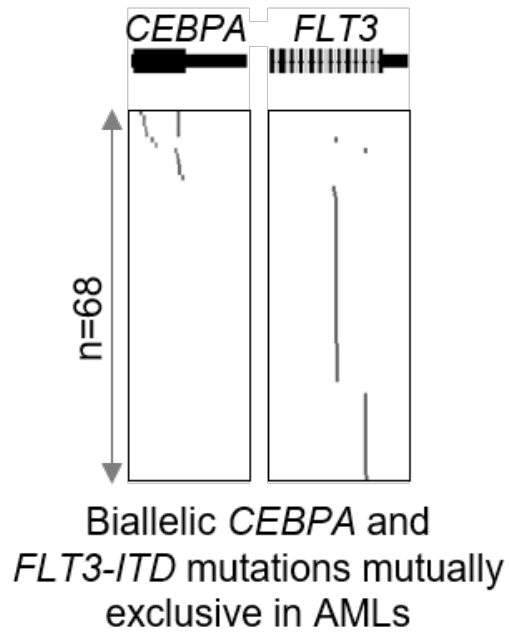
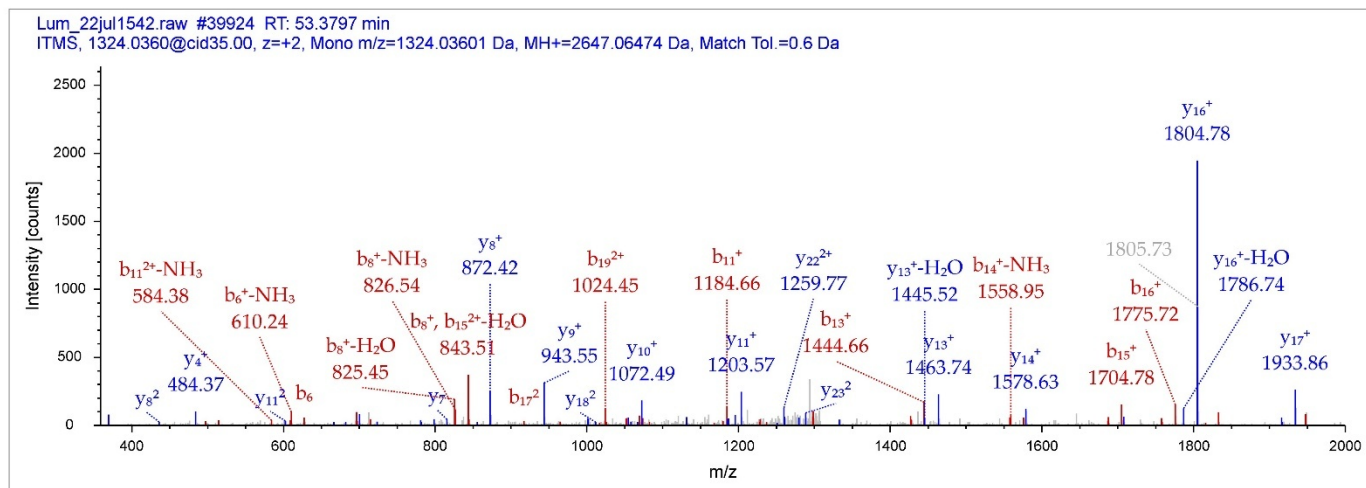


## SUPPLEMENTARY FIGURES

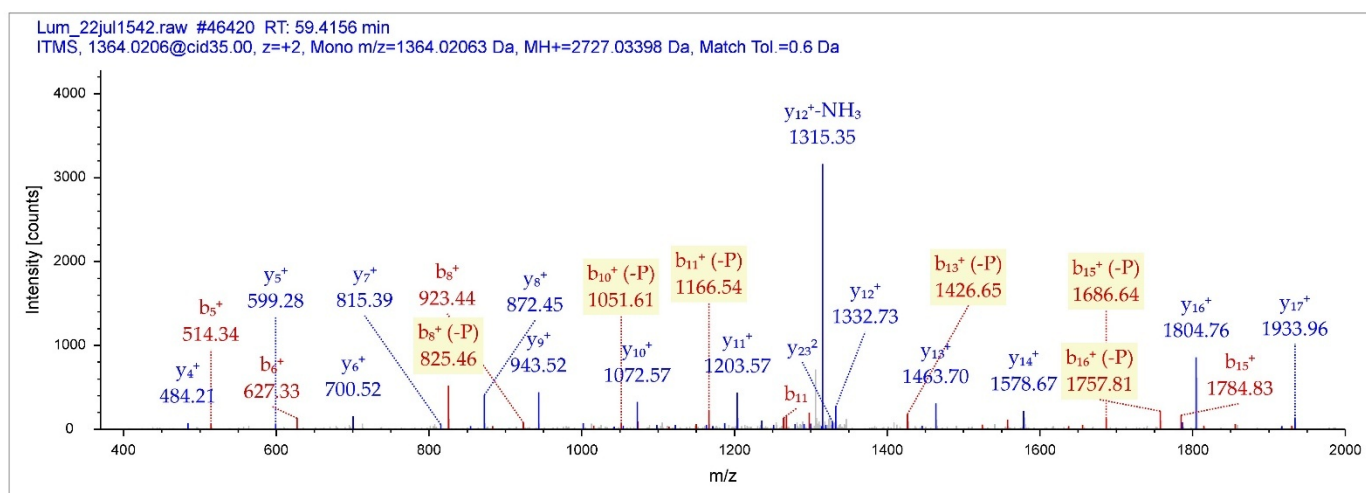


**Figure S1. *FLT3* mutations and *CEBPA* bi-allelic mutations are mutually exclusive.** Mutation calls from TCGA indicated by grey dots, primary AMLs with either *CEBPA* or *FLT3* mutations shown, *n*=68 (TCGA public data).

USP7 with unmodified serine 18:  
AGEQQL**S**EPEDMEMEAGDTDDPPR XCorr = 5.33

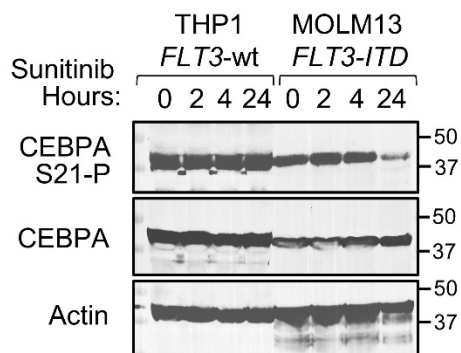


USP7 with phosphorylation of serine 18 (S18-P):  
AGEQQL**S(p)**EPEDMEMEAGDTDDPPR XCorr = 5.12

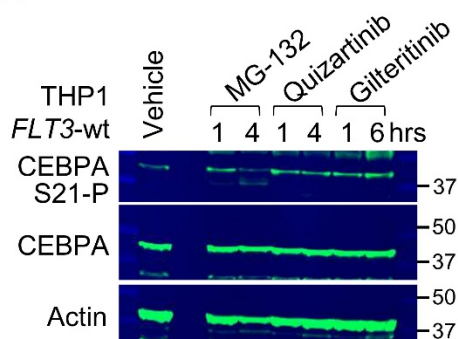


**Figure S2. USP7 phosphorylation at serine-18.** Tandem mass spectrum of unmodified and modified peptide AGEQQLSEPEDMEMEAGDTDDPPR. Phosphorylation at the position 7 serine in the peptide corresponds to serine 18 (S18) in USP7 protein. Xcorr = Sequest score that matches spectra to peptide sequences.

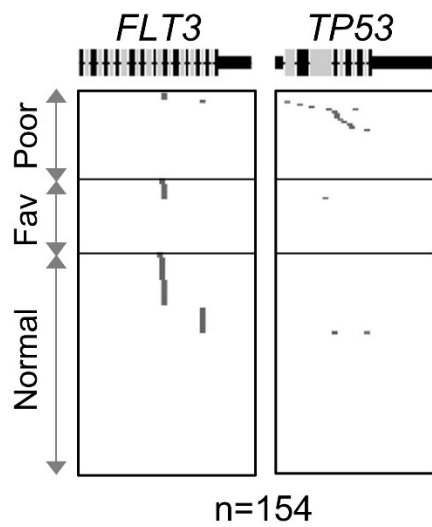
A



B

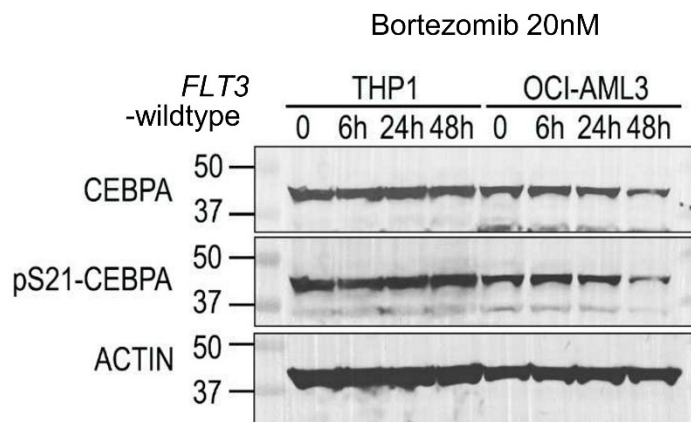


**Figure S3. TKI-treatments did not decrease CEBPA S21-P or increase total CEBPA in *FLT3*-wildtype (wt) AML cells. A) TKI treatment of *FLT3*-ITD AML cells (MOLM13) versus *FLT3*-wt AML cells (THP1). The cells were treated with vehicle or sunitinib 50 nM and harvested at time-points between 0-24 hours for Western blot analyses. B) *FLT3*-wt AML cells (THP1) treated with the UPP-inhibitor MG132 500nM, TKI quizartinib 0.5nM or TKI gilteritinib 10nM. Cells were harvested for Western blots between 1-6 hours after addition of the drugs.**

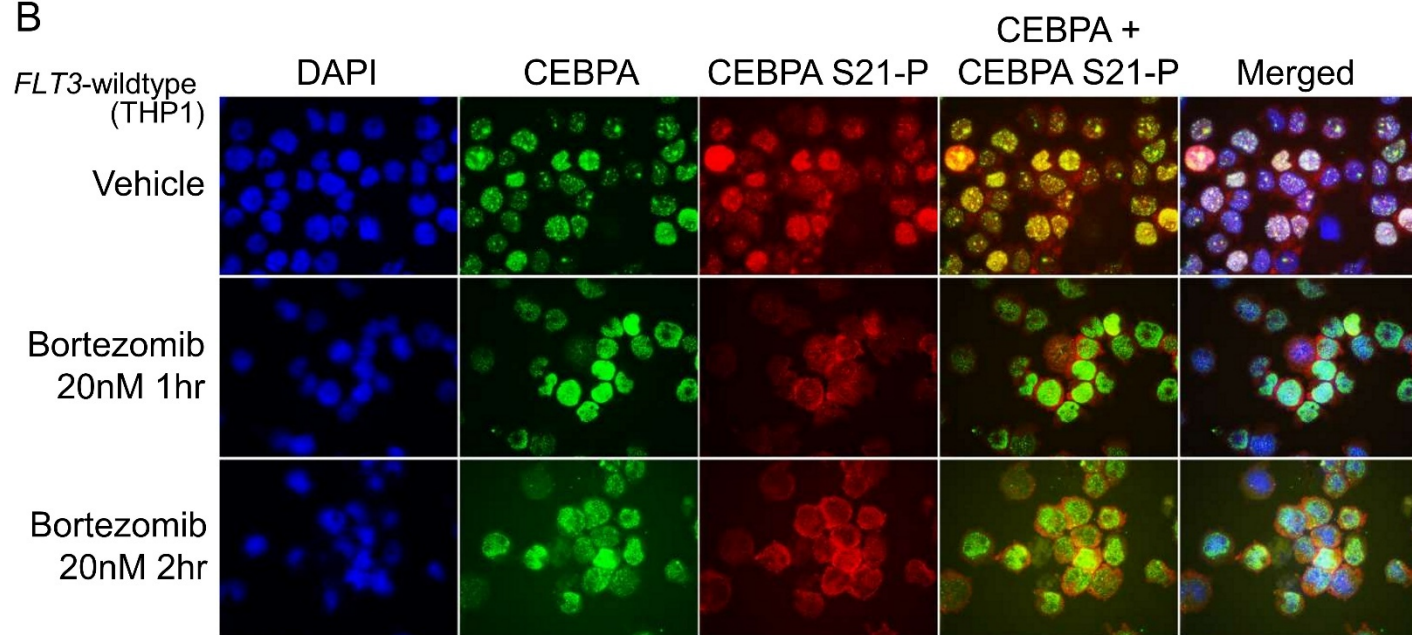


**Figure S4. *FLT3* and *TP53* mutations in AMLs are mutually exclusive, including in the sub-group of AMLs with complex cytogenetics ('poor') in which *TP53* mutations are particularly recurrent (The Cancer Genome Atlas [TCGA] public data).**

A



B



**Figure S5. The UPP-inhibitor bortezomib (UPP-inhibitor MG-132 data in Figure S2) did not increase CEBPA or CEBPA S21-P in *FLT3*-wildtype AML cells THP1 and OCI-AML3. A) Western blots in bortezomib-treated THP1 and OCI-AML3 cells. Concentration and time-points indicated in figure. B) Western blots in MG132-treated THP1 cells. C) Immunofluorescence for CEBPA and CEBPA S21-P in bortezomib-treated THP1 cells. Nuclei stained with DAPI. Images by Nikon Eclipse 400 microscope; original magnification,  $\times 630$ .**