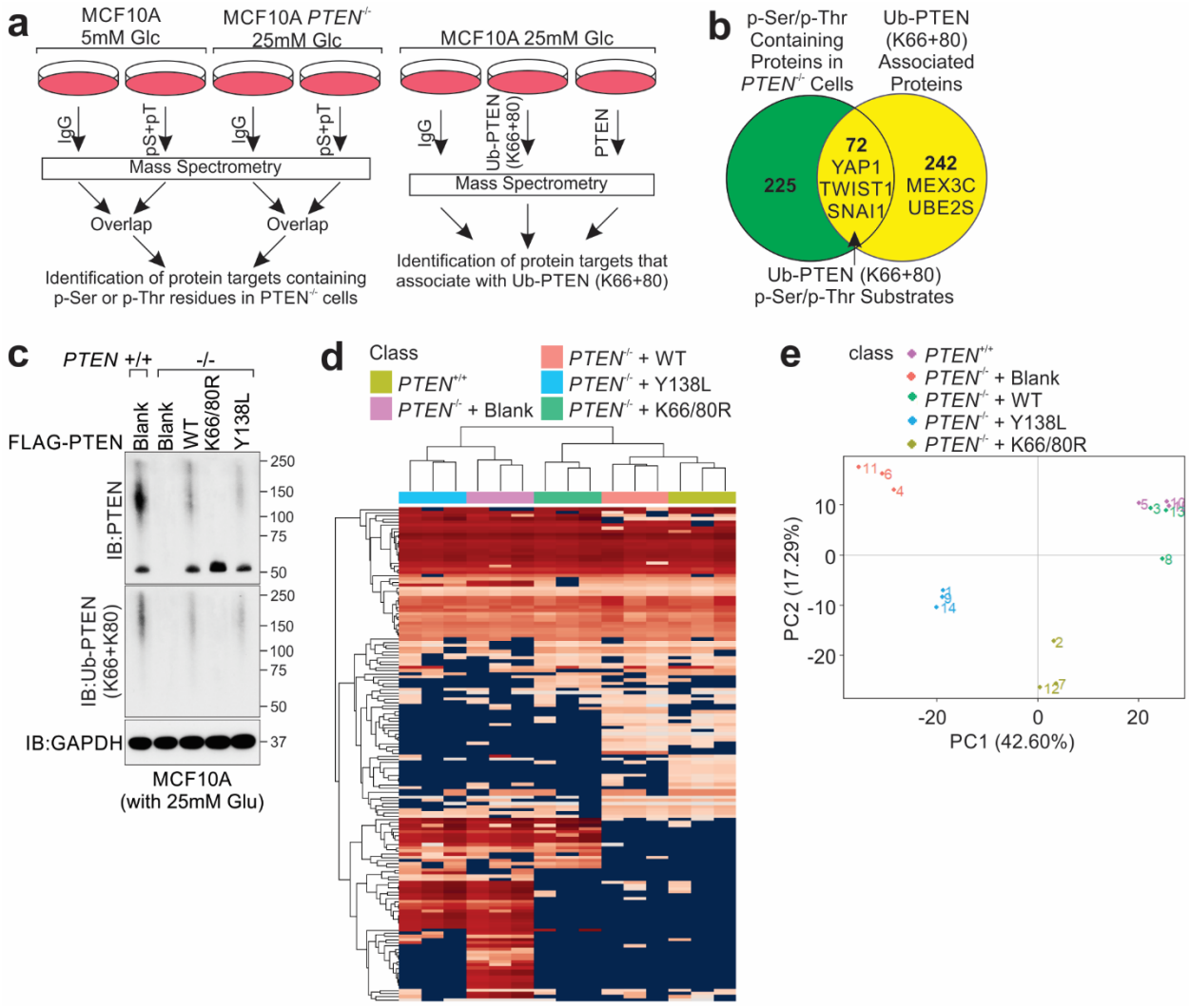

Figure S10: Characterization of PTEN$^{K27\text{-}polyUb}$ substrates.

(**a**) Experimental scheme of global identification of p-Ser/p-Thr-containing substrates that dephosphorylated by polyubiquitinated PTEN. (**b**) Overlapping of PTEN$^{K27\text{-}polyUb}$ binding proteins (*n*=242) in MCF10A cells with p-Ser/p-Thr-containing proteins enriched in MCF10A PTEN$^{-/-}$ cells (*n*=225). (**c**) Immunoblotting detection of PTEN ubiquitination using indicated antibodies of MCF10A *PTEN*$^{+/+}$, MCF10A *PTEN*$^{-/-}$ expressing blank vector, PTEN WT, Y138L or K80R mutants. (**d**) Heatmap depicting the Log[intensity] of from the MCF10A *PTEN*$^{+/+}$, MCF10A *PTEN*$^{-/-}$ expressing blank vector, PTEN WT, Y138L or K80R mutants. Columns and rows are reordered by hierarchical clustering using the genotype and experimental conditions. (**e**) Principle

component analysis (PCA) based on all proteomic features. The five experimental condition of three biological repeats were numbered as 1-15. X and Y axis show principal component 1 and principal component 2 that explain 17.29% and 42.60% of the total variance respectively. Prediction ellipses are such that a new observations from the same group will fall inside the ellipse with a probability of 0.95.