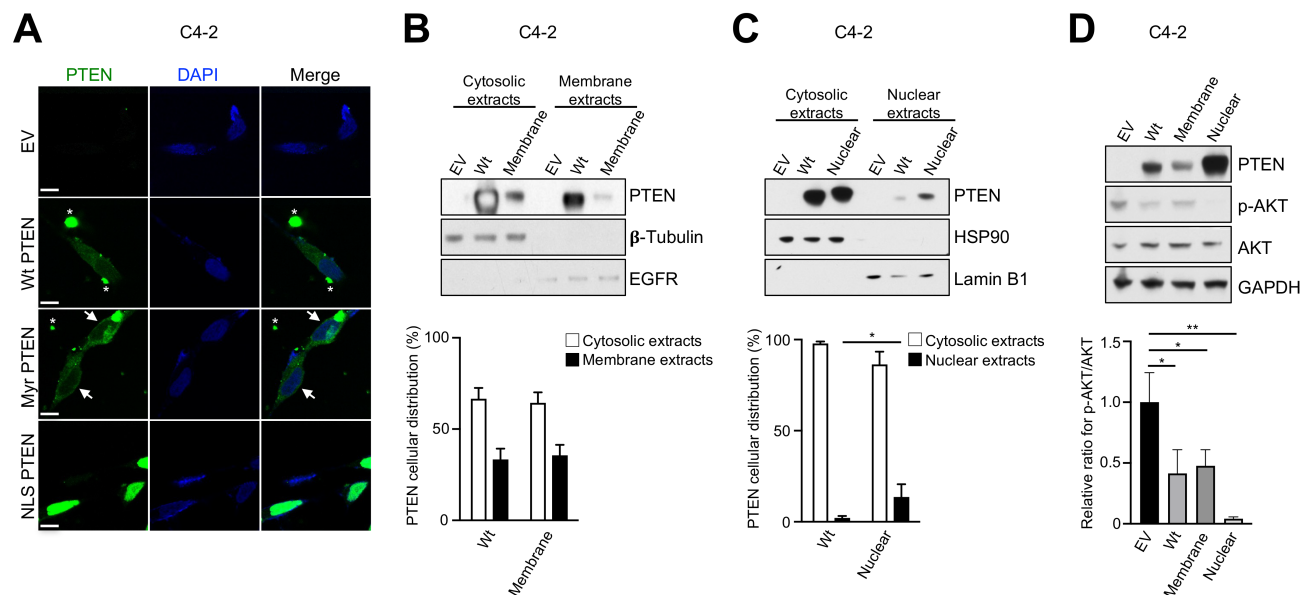
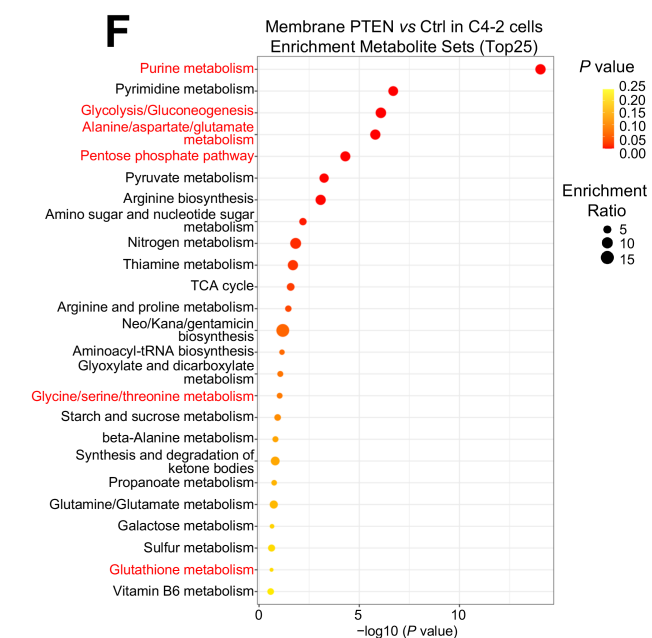
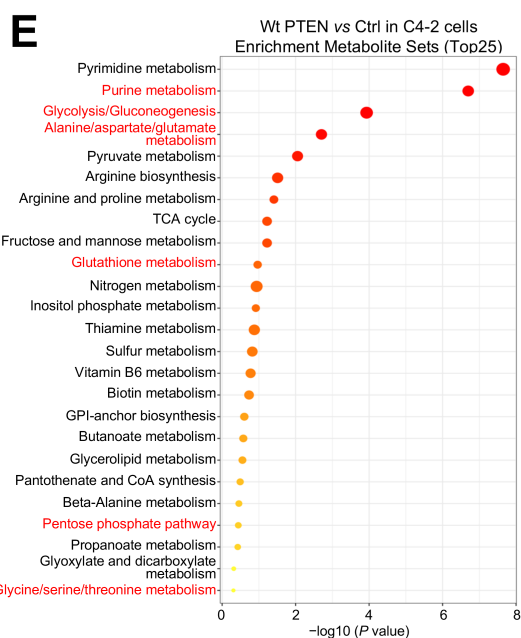
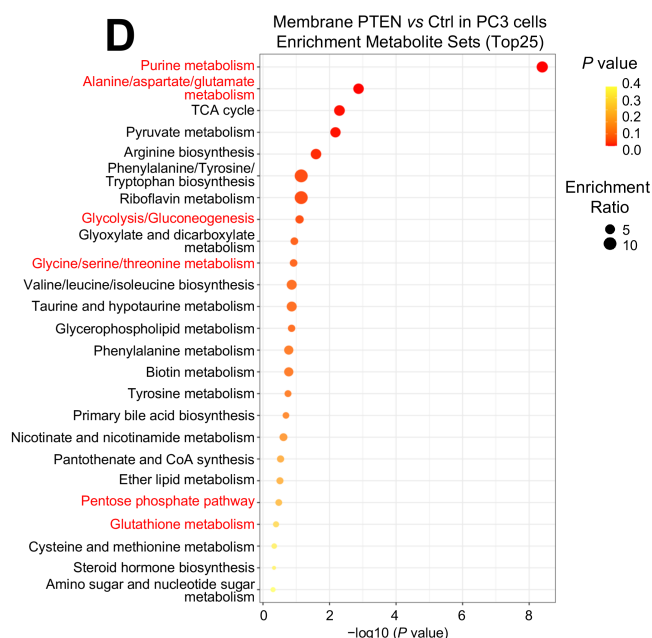
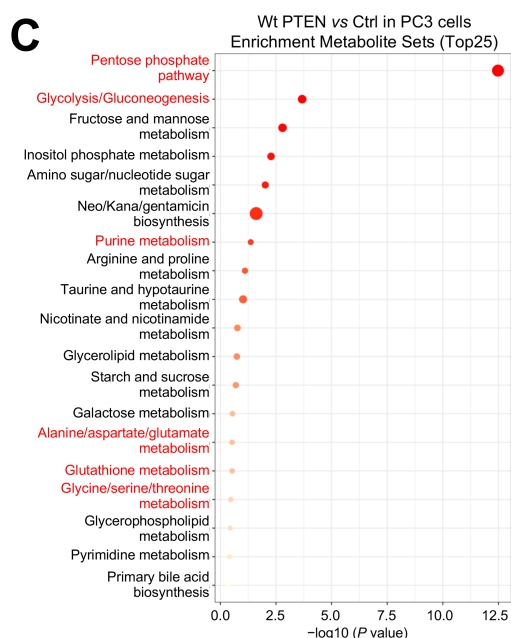
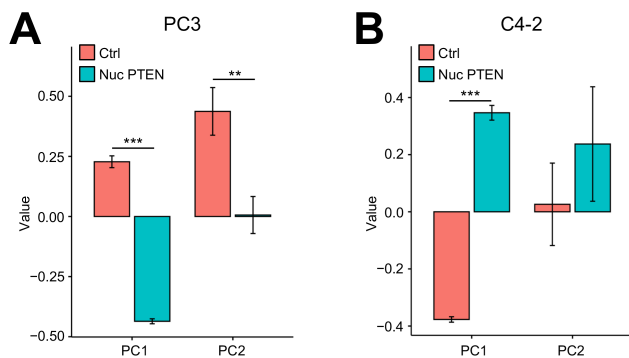


## Supplementary Data



**Supplementary Figure 1.** Establishment and validation of prostate cancer cell line inducibly overexpressing PTEN targeted to the plasma membrane and nucleus. **(A)** Immunofluorescent staining of PTEN in PTEN inducible C4-2 stable cell lines. Myr, myristoylated. Arrows indicate focal PTEN staining at the plasma membrane. Stars indicate non-specific fluorescent dye staining. Scale bars, 20  $\mu$ m. **(B–D)** IB analysis of C4-2 lysates from cytosolic and membrane extracts **(B)**, cytosolic and nuclear extracts **(C)**, or regular whole-cell extracts **(D)**. In **A–D**, EV, empty vector. In **B** and **C**, quantification of the band intensity was carried out with ImageJ. After normalized against its respective markers, the percentage of PTEN protein in cytosolic, membrane, or nuclear extracts was calculated against total PTEN protein. \* $P < 0.05$ , \*\* $P < 0.01$ . All data are mean  $\pm$  SD from  $n = 3$  biological replicates.



**Supplementary Figure 2.** Wt and membrane PTEN shared several commonly enriched metabolic pathways. **(A, B)** The statistical analysis of the first and second components between control and nuclear PTEN-overexpressed PC3 **(A)** and C4-2 cells **(B)**. **(C, D)** Over-representation analysis of significantly changed metabolites in Wt PTEN **(C)** and membrane PTEN **(D)** overexpressed PC3 cells, compared to its control counterpart. **(E, F)** Over-representation analysis of significantly changed metabolites in Wt PTEN **(E)** and membrane PTEN **(F)** overexpressed C4-2 cells, compared to its control counterpart. Six commonly enriched metabolic pathways, including glycolysis and purine metabolism, in all Wt and membrane PTEN-overexpressed cell lines are highlighted in Red.  $**P < 0.01$ ,  $***P < 0.001$ . All data are mean  $\pm$  SD from  $n = 3$  biological replicates.