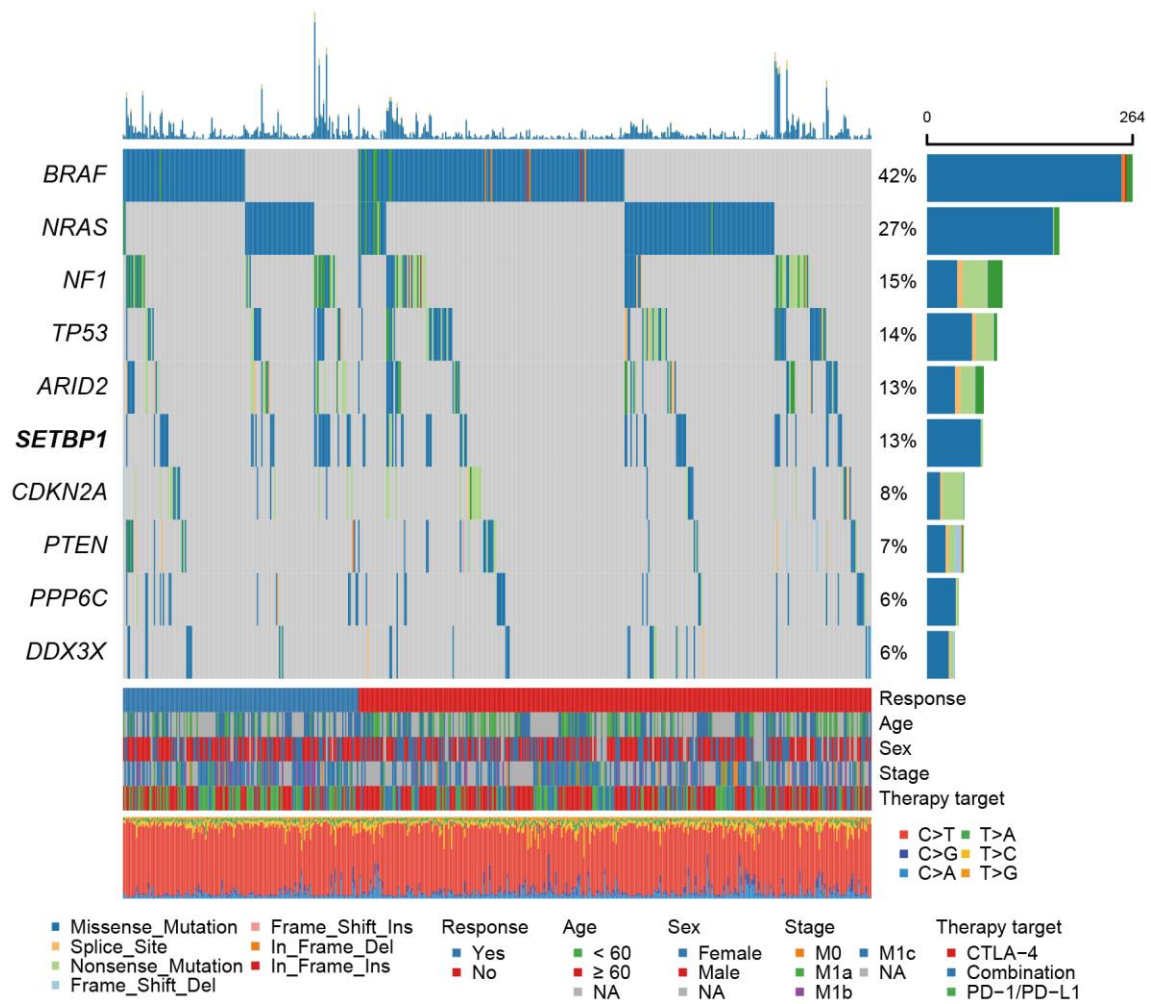
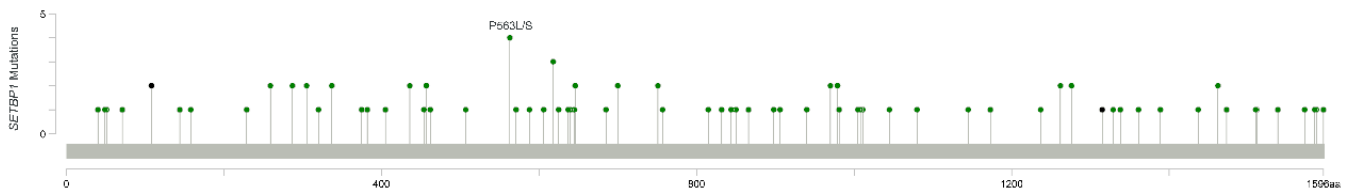


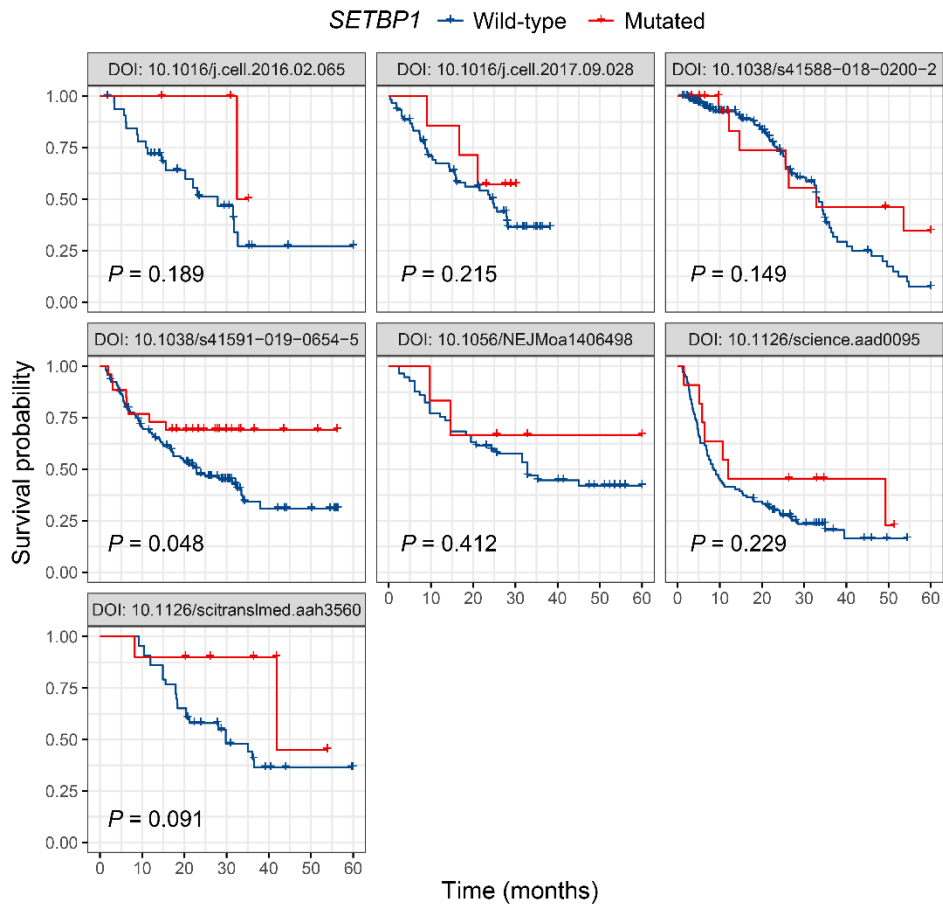
**SUPPLEMENTARY FIGURES**



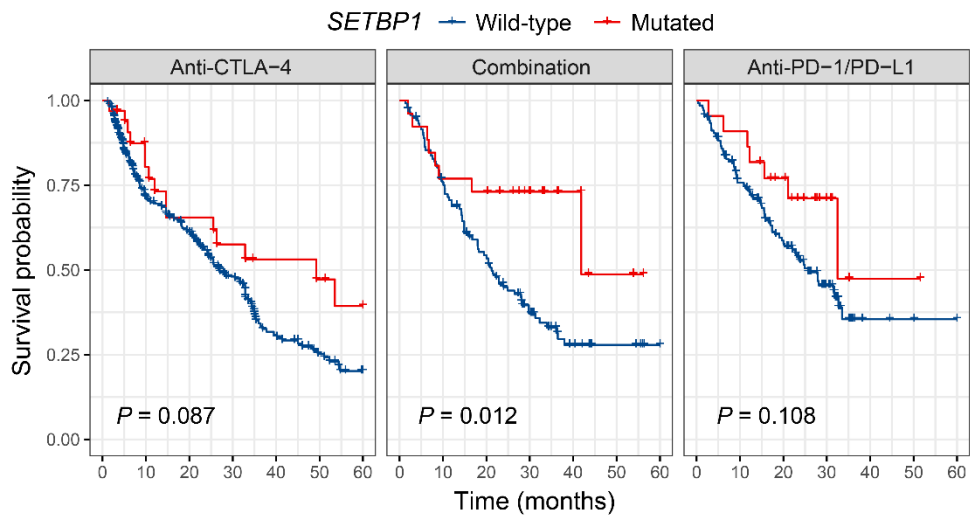
**Supplementary Figure 1. Mutational patterns of SETBP1 and common melanoma driver genes illustrated with waterfall plot.**



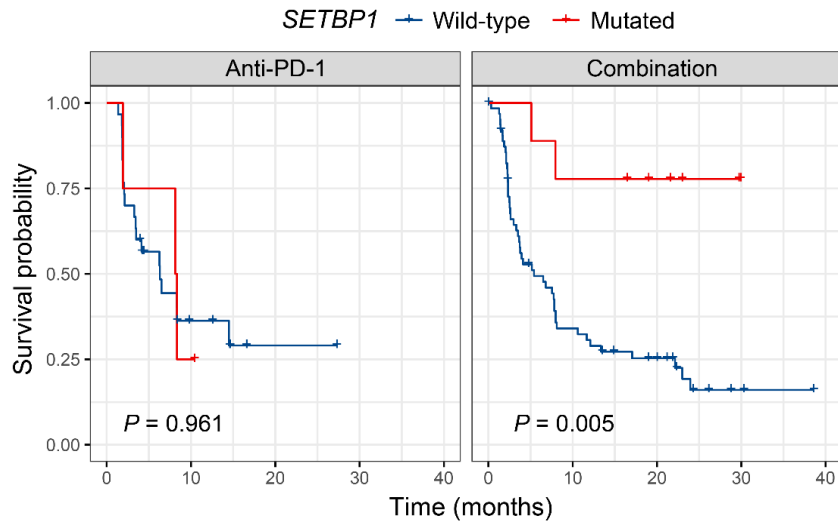
**Supplementary Figure 2. Detailed amino acid changes induced by SETBP1 mutations in the integrated melanoma cohort.**



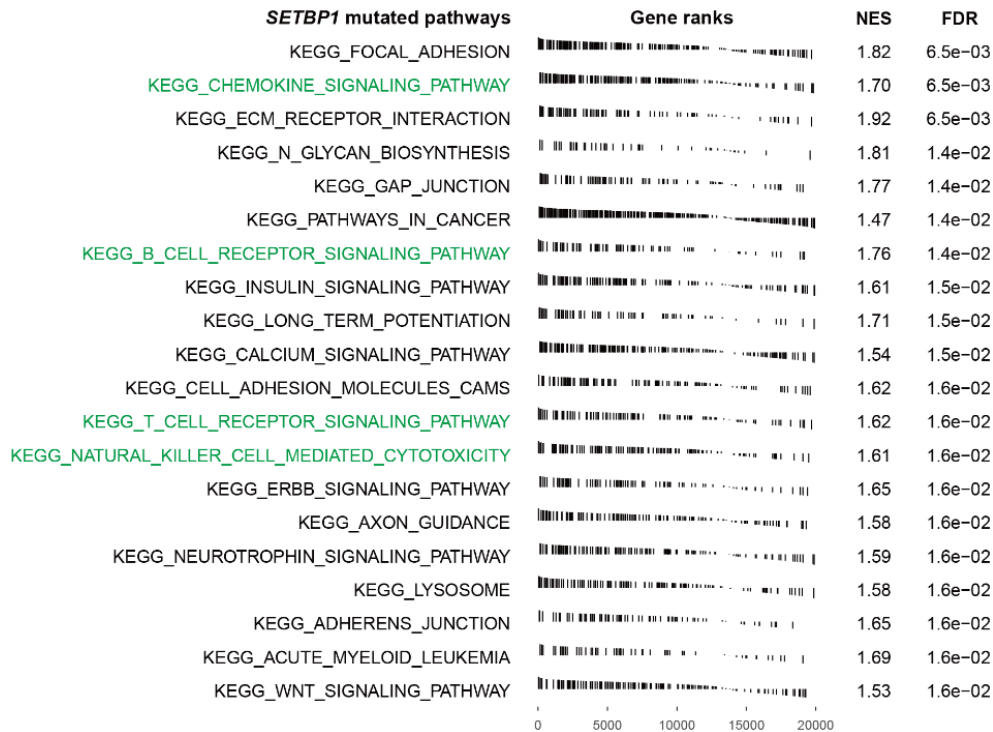
**Supplementary Figure 3. Kaplan-Meier survival analyses of SETBP1 mutations in individual ICI-treated melanoma cohorts.**



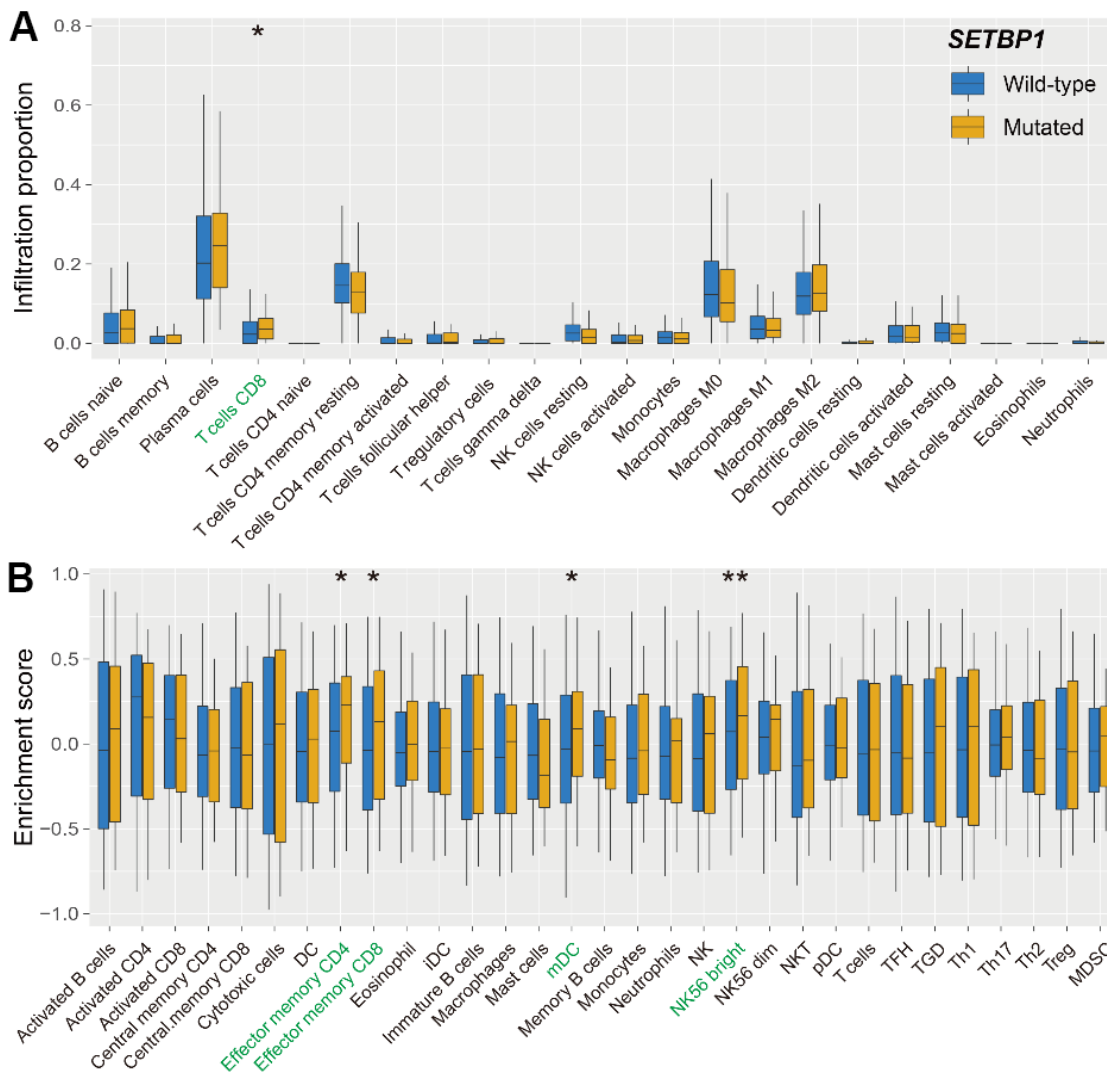
**Supplementary Figure 4. Kaplan-Meier survival analyses of SETBP1 mutations in distinct ICI treatment types in melanoma.**

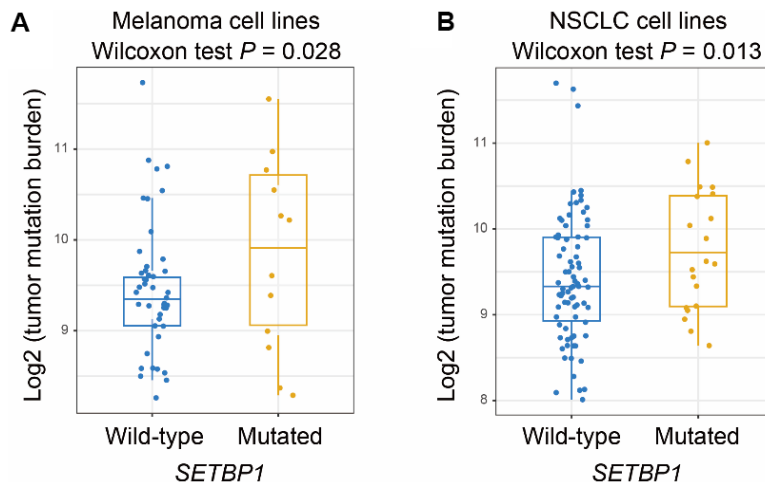


Supplementary Figure 5. Kaplan-Meier survival analyses of SETBP1 mutations in individual ICI-treated NSCLC cohorts.

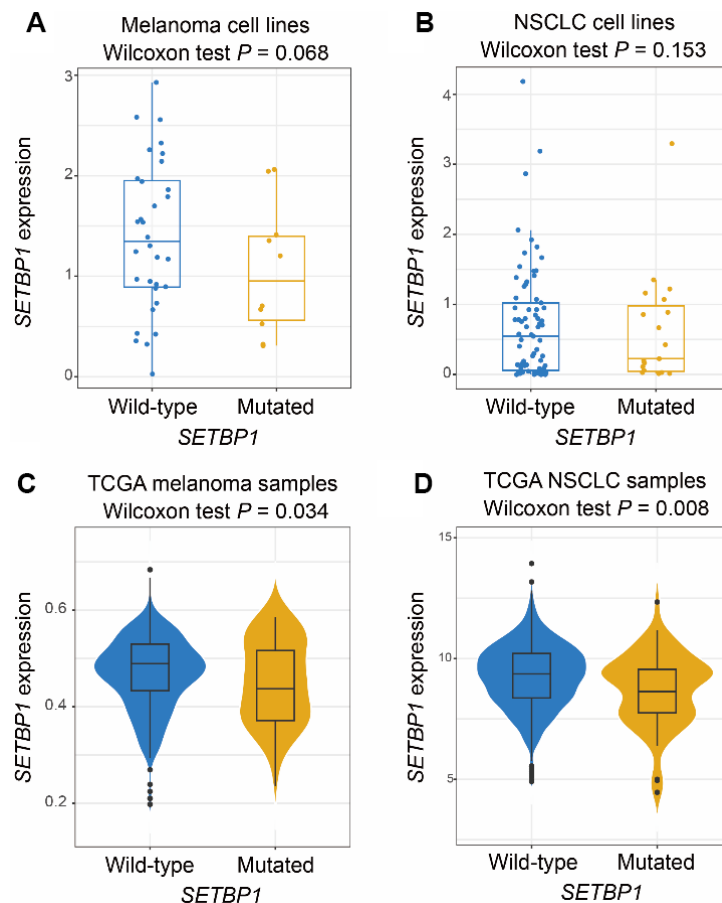


Supplementary Figure 6. Significantly enriched signaling pathways in SETBP1 mutated subgroups in melanoma. Immune response pathways were highlighted with green.

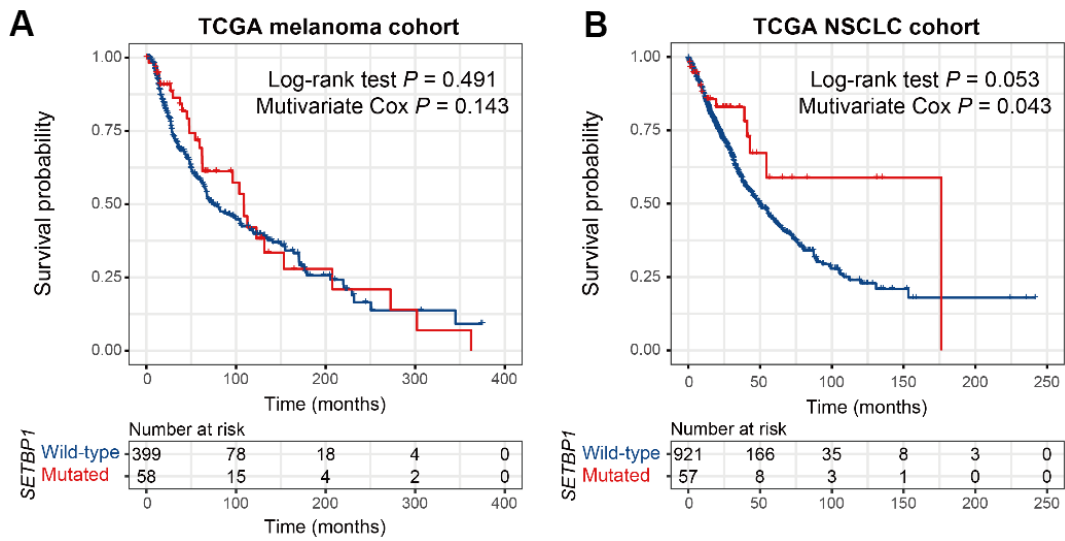




**Supplementary Figure 8. Associations between SETBP1 mutations and TMB in CCLE-derived cell lines for melanoma and NSCLC.** (A) Distinct TMB distribution in SETBP1 mutated and wild-type subgroups based on 57 melanoma cell lines. (B) Distinct TMB distribution in SETBP1 mutated and wild-type subgroups based on 98 NSCLC cell lines.



**Supplementary Figure 9. Associations between SETBP1 mutations and its own expression.** (A) Distinct SETBP1 expression in SETBP1 mutated and wild-type subgroups based on 42 melanoma cell lines. (B) Distinct SETBP1 expression in SETBP1 mutated and wild-type subgroups based on 92 NSCLC cell lines. (C) Distinct SETBP1 expression in SETBP1 mutated and wild-type subgroups based on TCGA melanoma samples. (D) Distinct SETBP1 expression in SETBP1 mutated and wild-type subgroups based on TCGA NSCLC samples.



**Supplementary Figure 10.** Prognostic capacities of SETBP1 mutations in (A) melanoma and (B) NSCLC patients derived from the TCGA project.