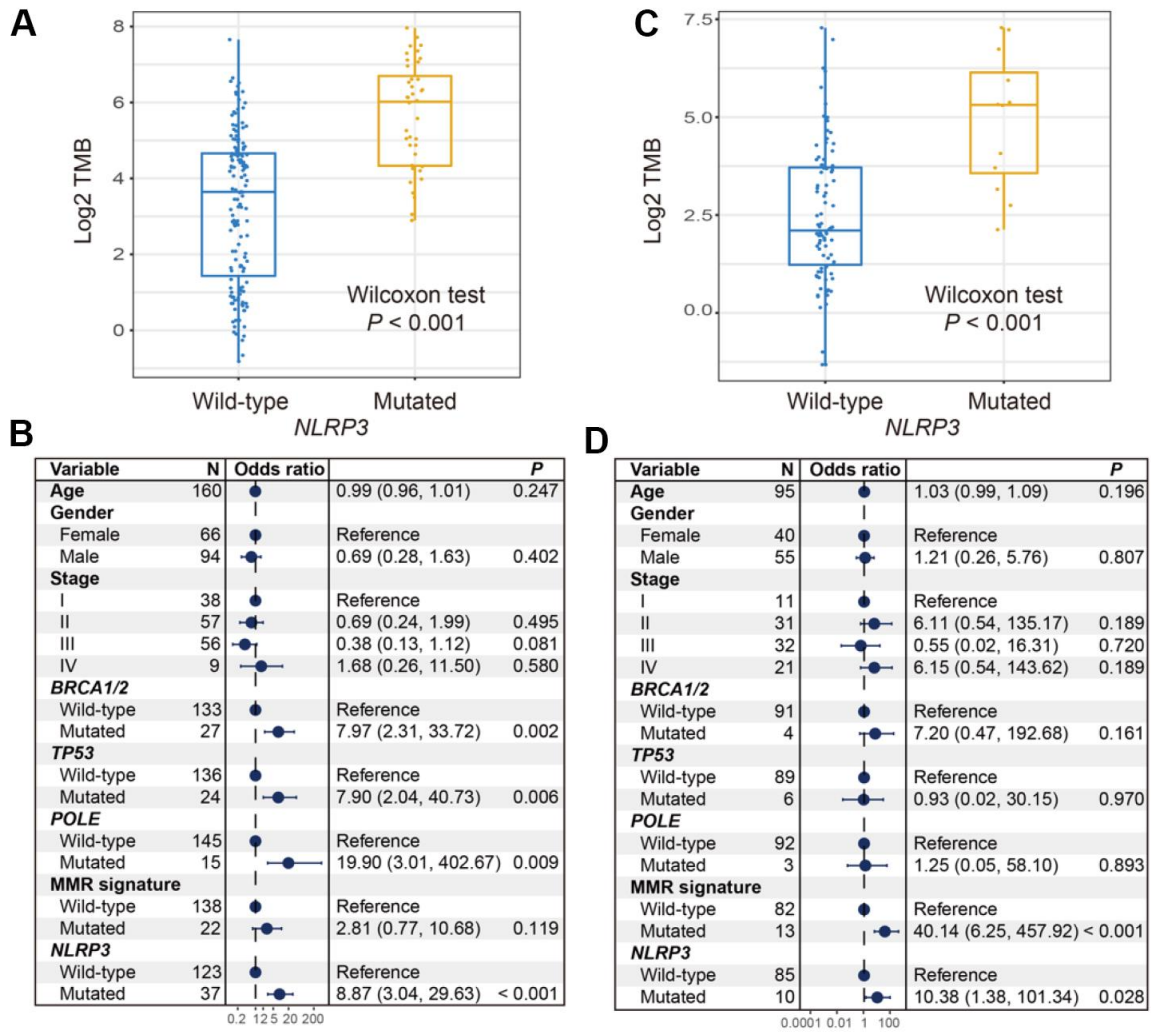
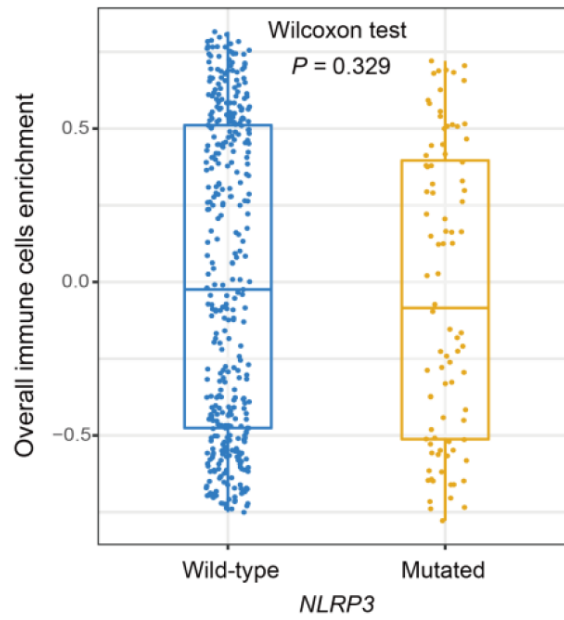


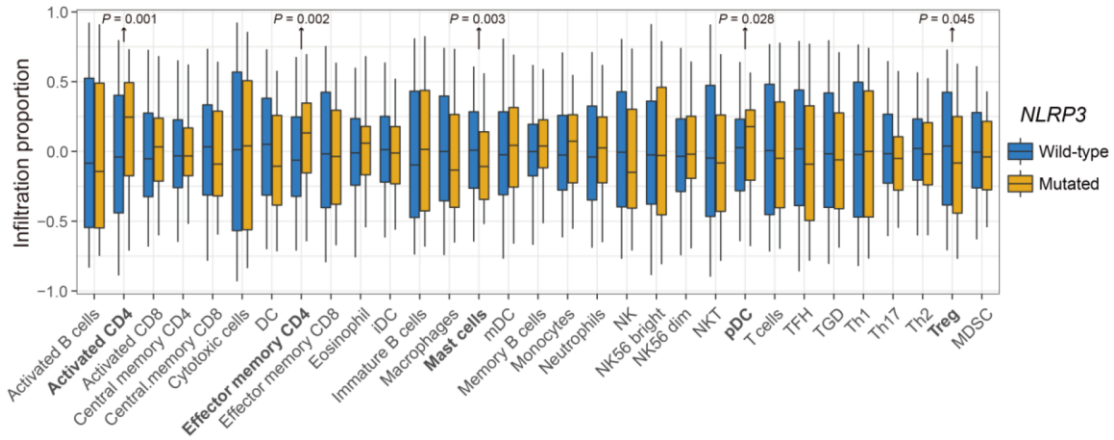
SUPPLEMENTARY FIGURES



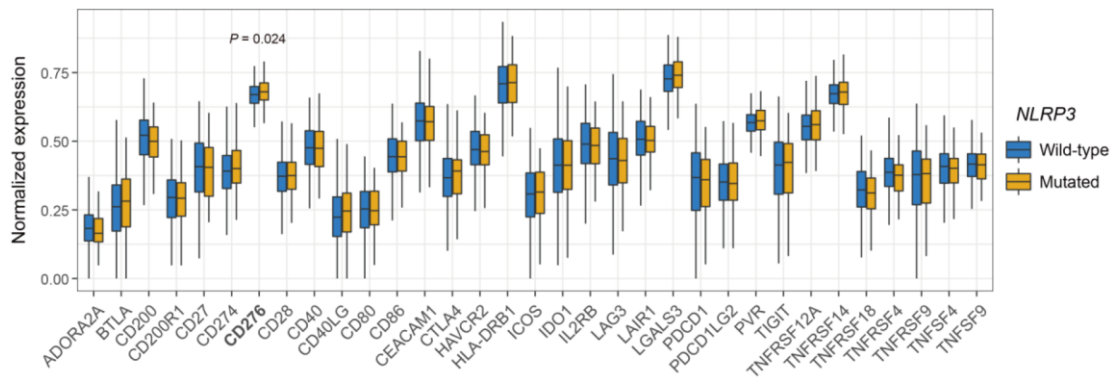
Supplementary Figure 1. Association of *NLRP3* mutations with TMB in 2 ICGC melanoma cohorts. *NLRP3* mutations versus TMB with (A) univariate analysis and (B) multivariate regression model in MELA-AU cohort; *NLRP3* mutations versus TMB with (C) univariate analysis and (D) multivariate regression model in SKCA-BR cohort.



Supplementary Figure 2. Infiltration of overall immune cells in patients with and without *NLRP3* mutations.



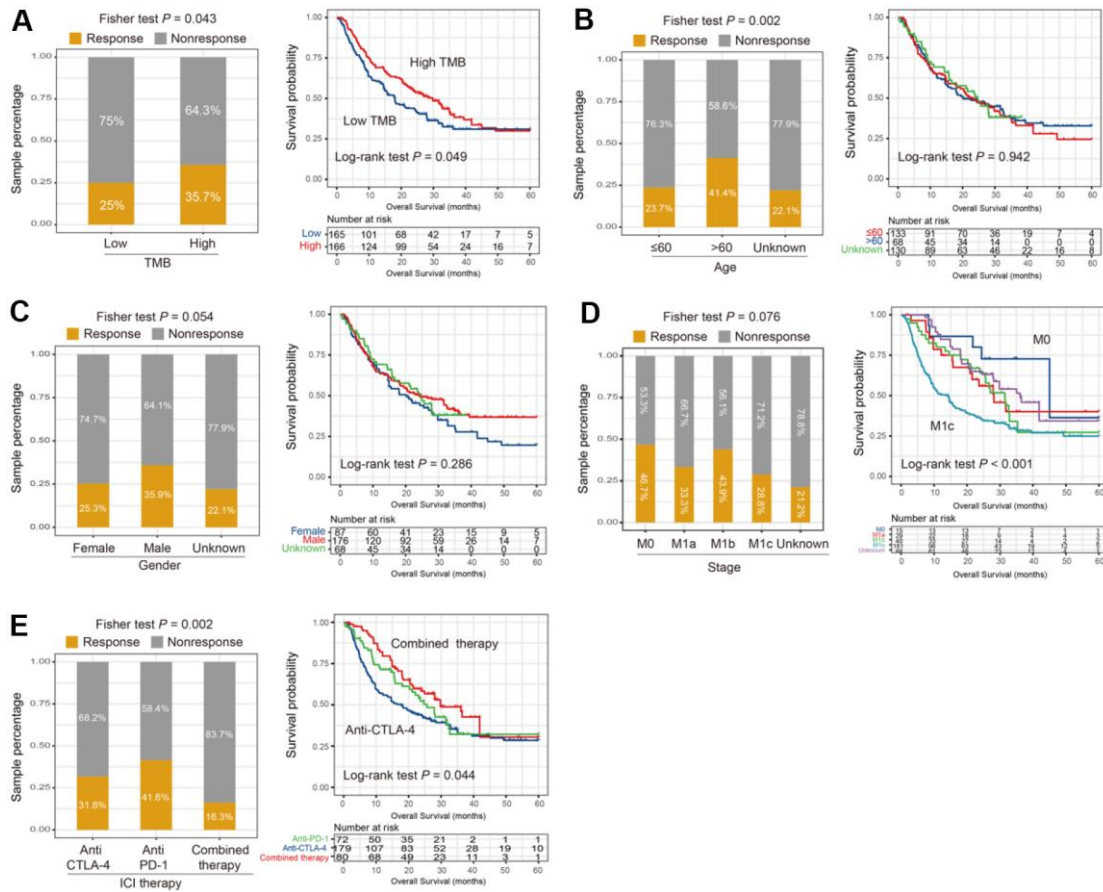
Supplementary Figure 3. Infiltration of 31 immune cells stratified by *NLRP3* mutation status according to Angelova et al. method.



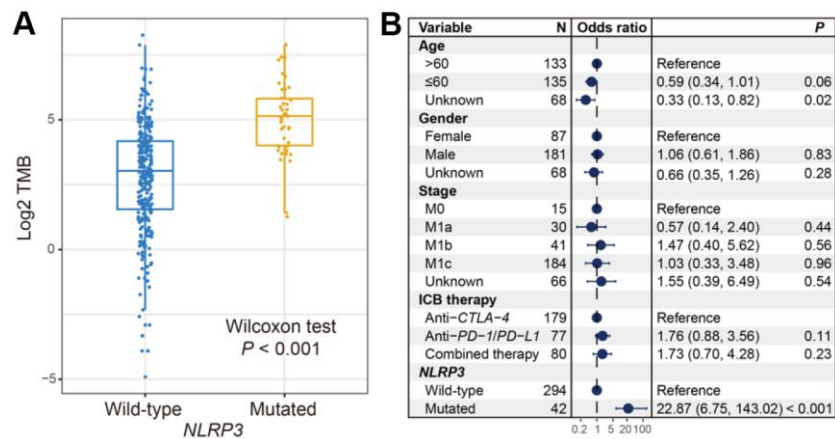
Supplementary Figure 4. Expression of 33 immune checkpoint genes stratified by *NLRP3* mutation status.

Mutated <i>NLRP3</i> pathways	Gene ranks	NES	<i>P</i>	FDR
ARACHIDONIC_ACID_METABOLISM		2.65	7.4e-04	5.7e-03
HEDGEHOG_SIGNALING_PATHWAY		1.86	7.3e-04	5.7e-03
BASAL_CELL_CARCINOMA		1.95	7.1e-04	5.7e-03
COMPLEMENT_AND_COAGULATION_CASCADES		2.36	8.7e-04	6.4e-03
LINOLEIC_ACID_METABOLISM		2.07	9.9e-04	7.0e-03
GRAFT_VERSUS_HOST_DISEASE		2.02	1.1e-03	7.1e-03
ECM_RECEPTOR_INTERACTION		2.11	1.0e-03	7.1e-03
CELL_ADHESION_MOLECULES_CAMS		1.63	1.7e-03	9.2e-03
ALLOGRAFT_REJECTION		1.74	5.4e-03	2.4e-02
CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION		2.08	5.7e-03	2.5e-02

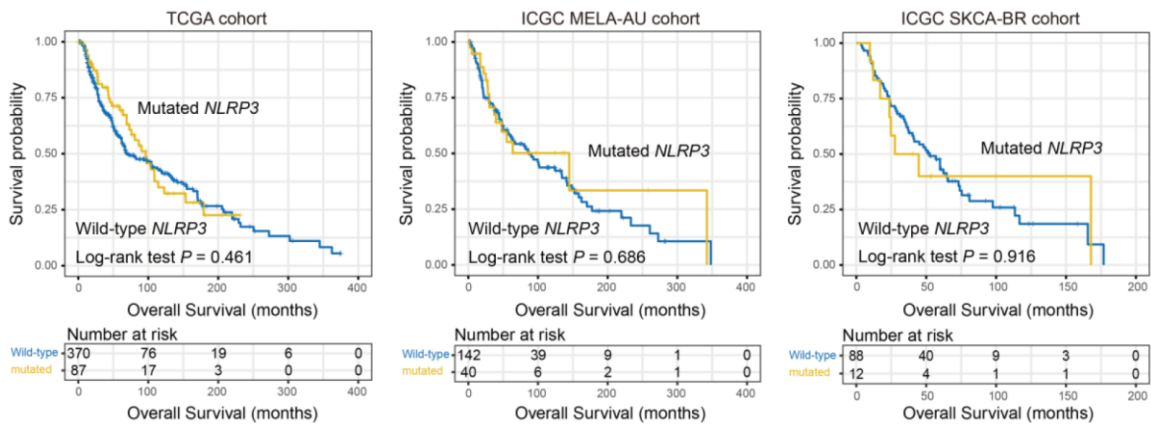
Supplementary Figure 5. GSEA analysis of *NLRP3* mutant patients.



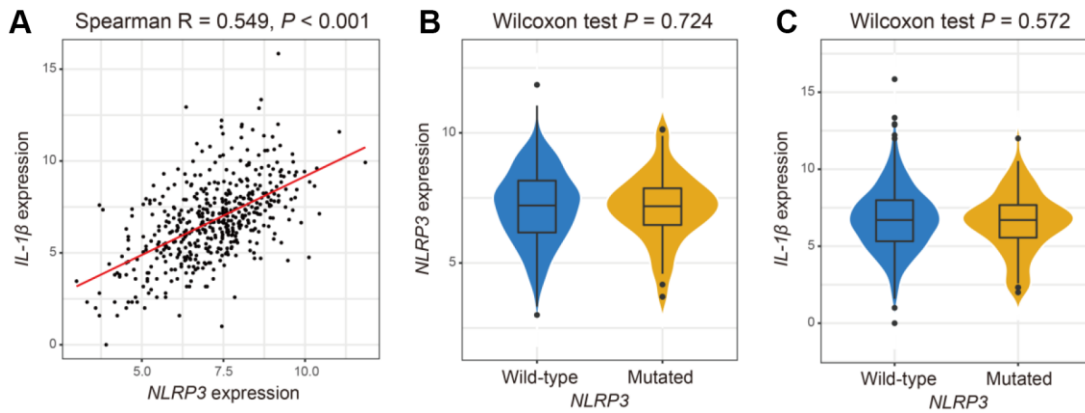
Supplementary Figure 6. Clinical characteristics association with ICI efficacy. Association of (A) TMB, (B) age, (C) gender, (D) stage, and (E) treatment type with ICI response rate and prognosis.



Supplementary Figure 7. Correlation of *NLRP3* mutations with TMB in the pooled ICI-treated cohort. (A) Wilcoxon rank-sum test and (B) multivariate Logistic regression analysis for the correlation of *NLRP3* mutations with TMB.



Supplementary Figure 8. Kaplan-Meier survival analysis of *NLRP3* mutations in 3 non-ICI-treated cohorts.



Supplementary Figure 9. *NLRP3* and *IL-1 β* mRNA expression concerning *NLRP3* mutational status in melanoma based on the data from TCGA cohort. (A) Correlation analysis between *NLRP3* and *IL-1 β* expression. Distinct expression of (B) *NLRP3* and (C) *IL-1 β* in *NLRP3* wild-type versus mutated subgroups.