

Supplementary Figures

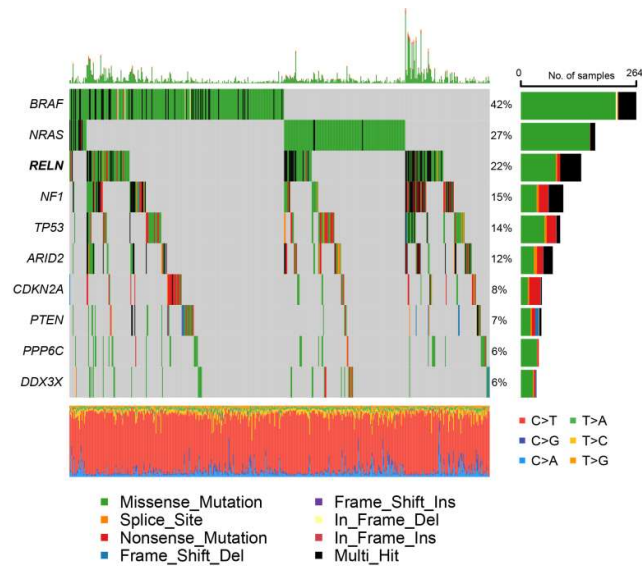


Figure S1. Mutational patterns of *RELN* and common melanoma driver genes exhibited with waterfall plot.

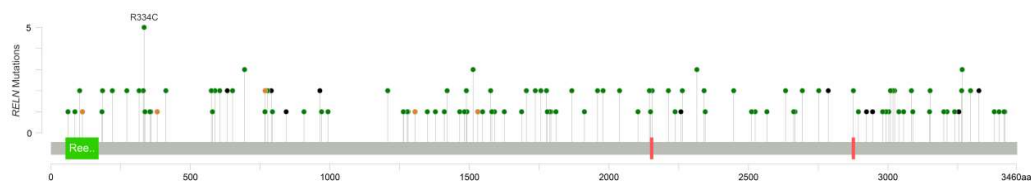


Figure S2. Detailed amino acid changes induced by *RELN* mutations in the integrated melanoma cohort.

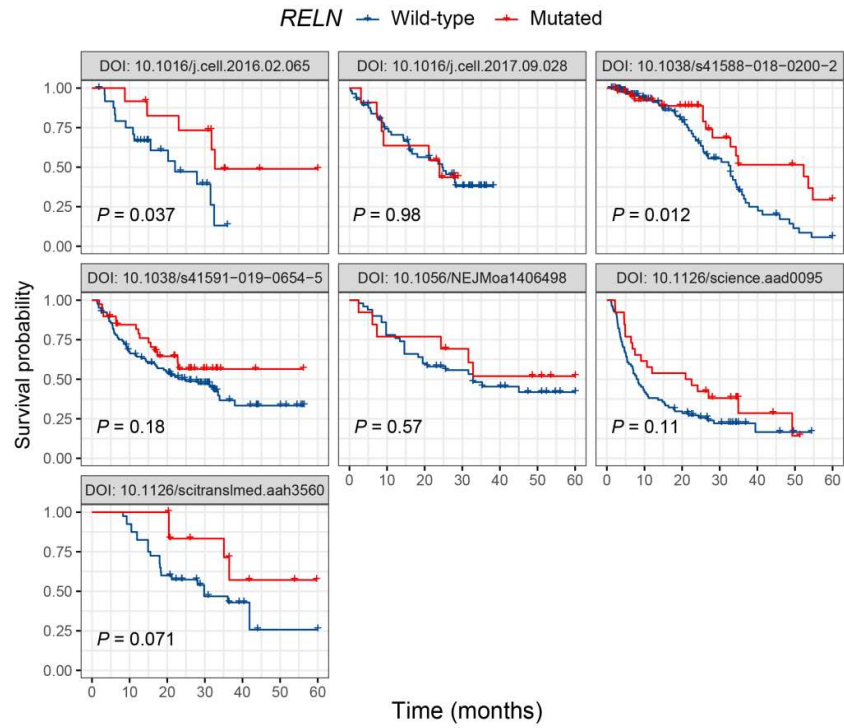


Figure S3. Kaplan-Meier survival analyses of *RELN* mutations in individual ICI-treated melanoma cohorts.

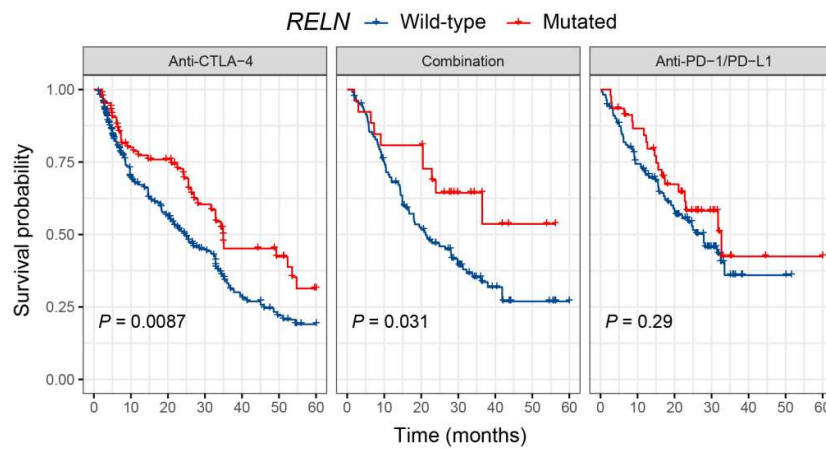


Figure S4. Kaplan-Meier survival analyses of *RELN* mutations in distinct ICI treatment types in melanoma.

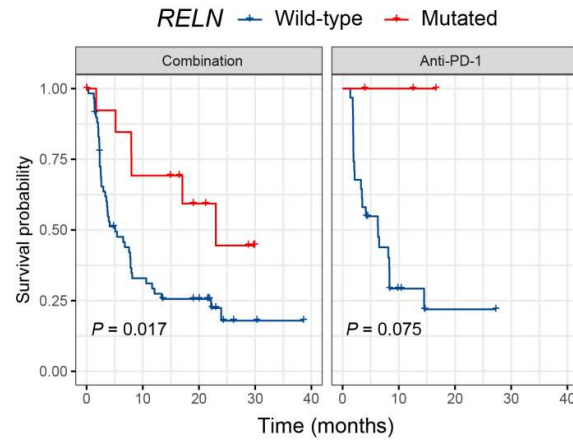


Figure S5. Kaplan-Meier survival analyses of *RELN* mutations in individual ICI-treated NSCLC cohorts.

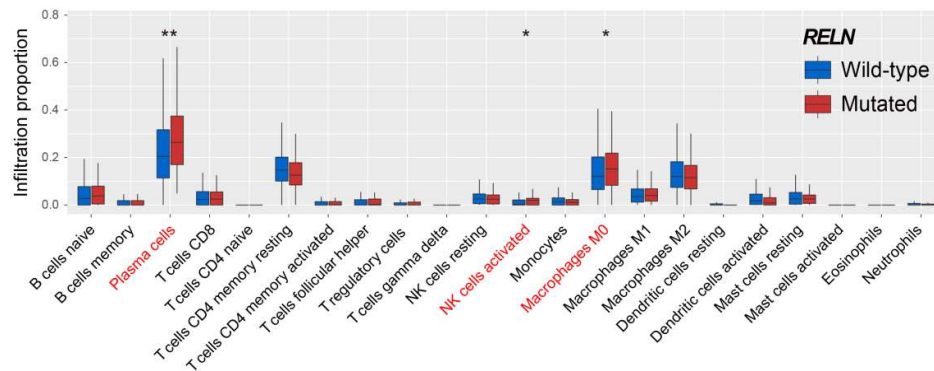


Figure S6. Distinct infiltration of 22 immunocytes of *RELN* mutated and wild-type groups evaluated with CIBERSORT algorithm in NSCLC. Immunocytes highlighted with red are significantly differentially infiltrated.

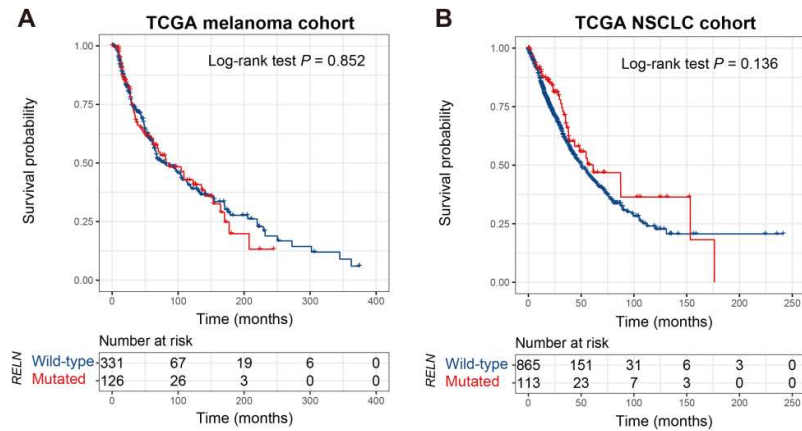


Figure S7. Prognostic capacities of *RELN* mutations in (A) melanoma and (B) NSCLC patients derived from the TCGA project.

Variable	N	Hazard ratio	P
Age			
> 60	184	Reference	
≤ 60	178	1.07 (0.80, 1.45)	0.642
Unknown	264	1.07 (0.77, 1.50)	0.676
Sex			
Female	199	Reference	
Male	359	0.90 (0.70, 1.15)	0.386
Unknown	68	1.16 (0.77, 1.74)	0.489
Stage			
M0	25	Reference	
M1a	37	1.58 (0.65, 3.84)	0.318
M1b	58	2.07 (0.91, 4.70)	0.083
M1c	289	3.03 (1.42, 6.48)	0.004
Unknown	217	1.60 (0.74, 3.47)	0.233
Therapy target			
CTLA-4	324	Reference	
Combination	144	0.84 (0.61, 1.15)	0.273
PD-1/PD-L1	158	0.76 (0.55, 1.07)	0.114
FAT1			
Wild-type	545	Reference	
Mutated	81	0.69 (0.52, 1.02)	0.037
BRCA1/2			
Wild-type	553	Reference	
Mutated	73	1.02 (0.69, 1.49)	0.926
TP53			
Wild-type	535	Reference	
Mutated	91	1.33 (0.97, 1.84)	0.079
POLE			
Wild-type	595	Reference	
Mutated	31	0.56 (0.29, 1.05)	0.072
RELN			
Wild-type	467	Reference	
Mutated	159	0.72 (0.54, 0.96)	0.026

Figure S8. Multivariable Cox regression analysis of *RELN* mutations was performed with multiple clinical confounding factors taken into consideration in melanoma.

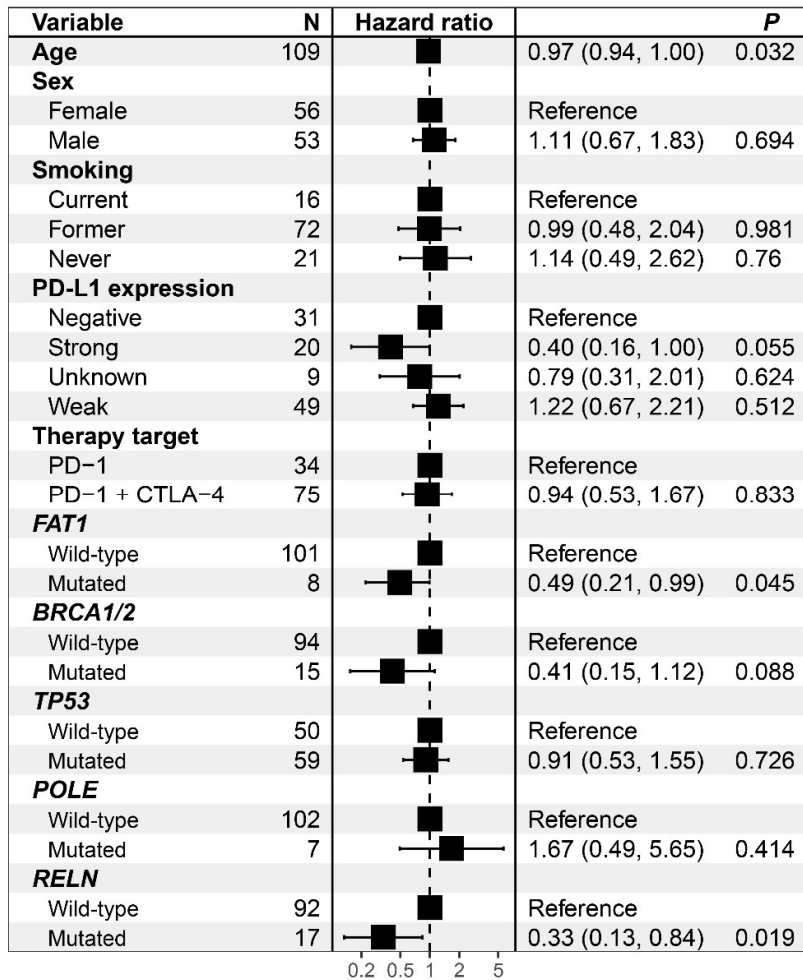


Figure S9. Multivariable Cox regression analysis of *RELN* mutations was performed with multiple clinical confounding factors taken into consideration in NSCLC.