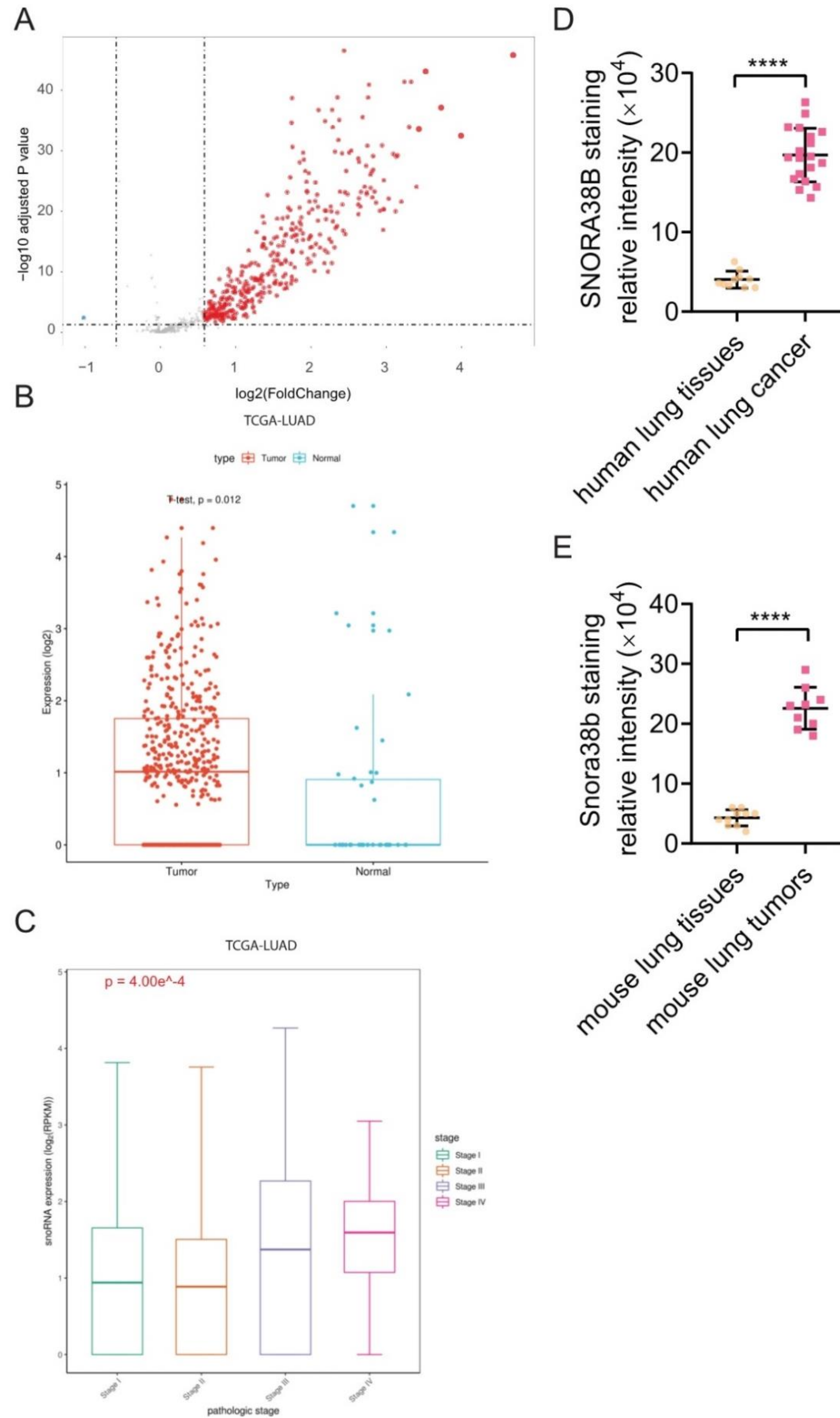
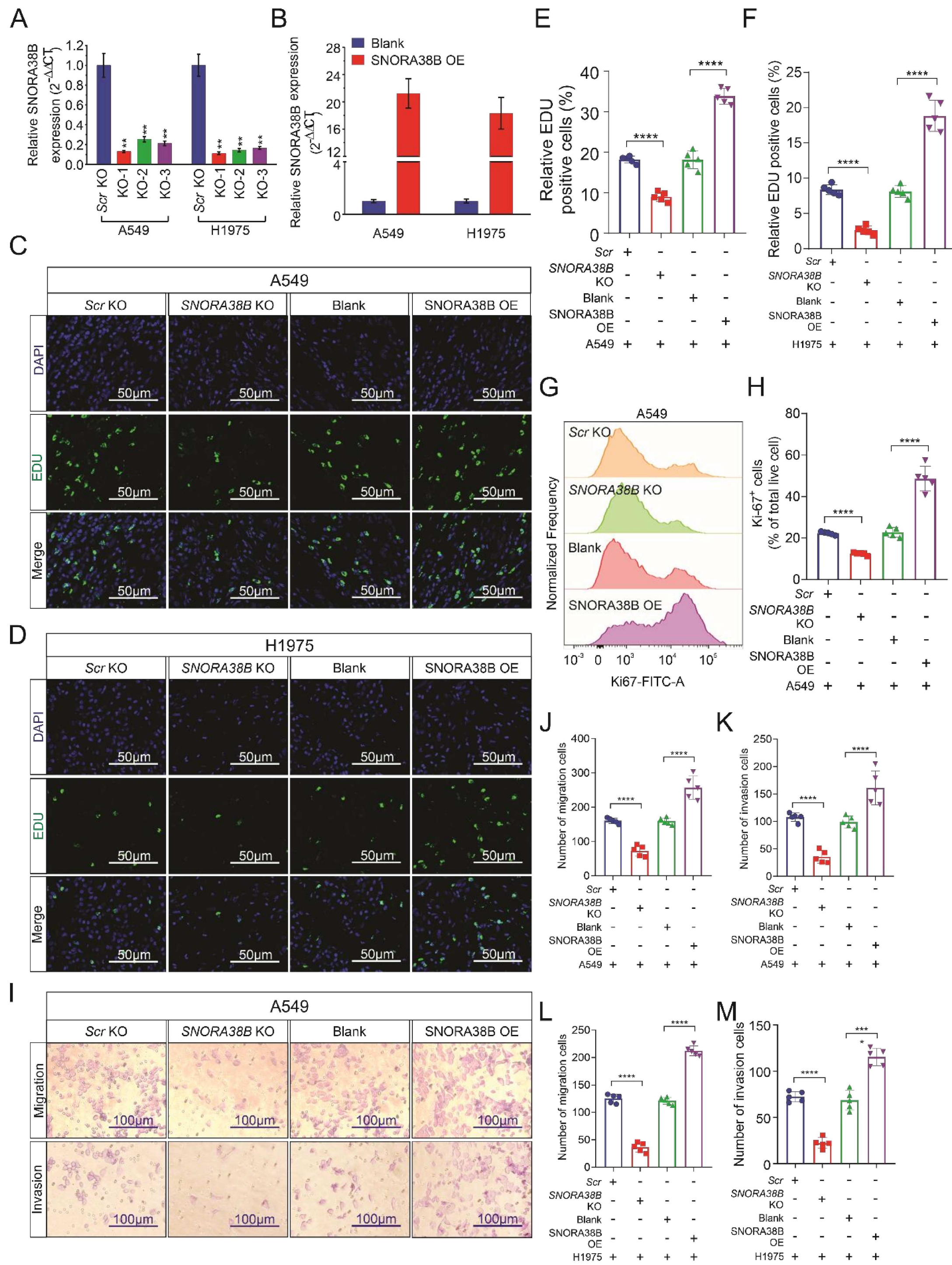
Supplemental Figure 1



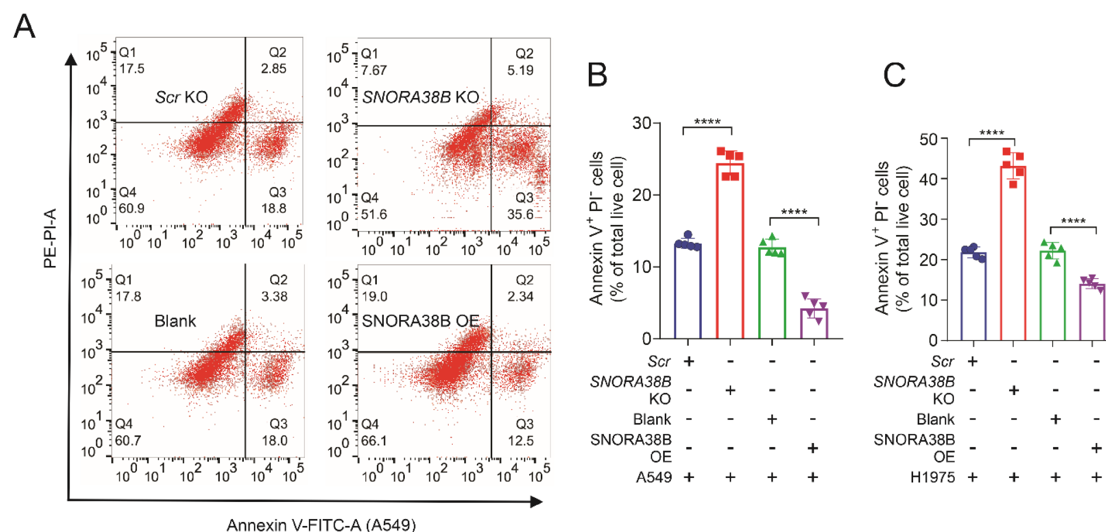
Supplemental Figure 1. SNORA38B was highly expressed in NSCLC and associated with poor prognosis. **A.** The volcanic map of differential gene expression between lung cancer tissue and adjacent normal lung tissues using TCGA database. Mapping by R software. **B.** Box plot of SNORA38B expression in tumor samples compared to adjacent normal sample using TCGA database. Mapping by R software. **C.** Box Plot of SNORA38B expression in different stages of NSCLC using TCGA database. Mapping by R software. **D-E.** Quantitatively results of RNA scope. ****$P < 0.0001$. Means ± SD were shown. Statistical analysis was performed by Student's t-test analysis.

Supplementary Figure 2



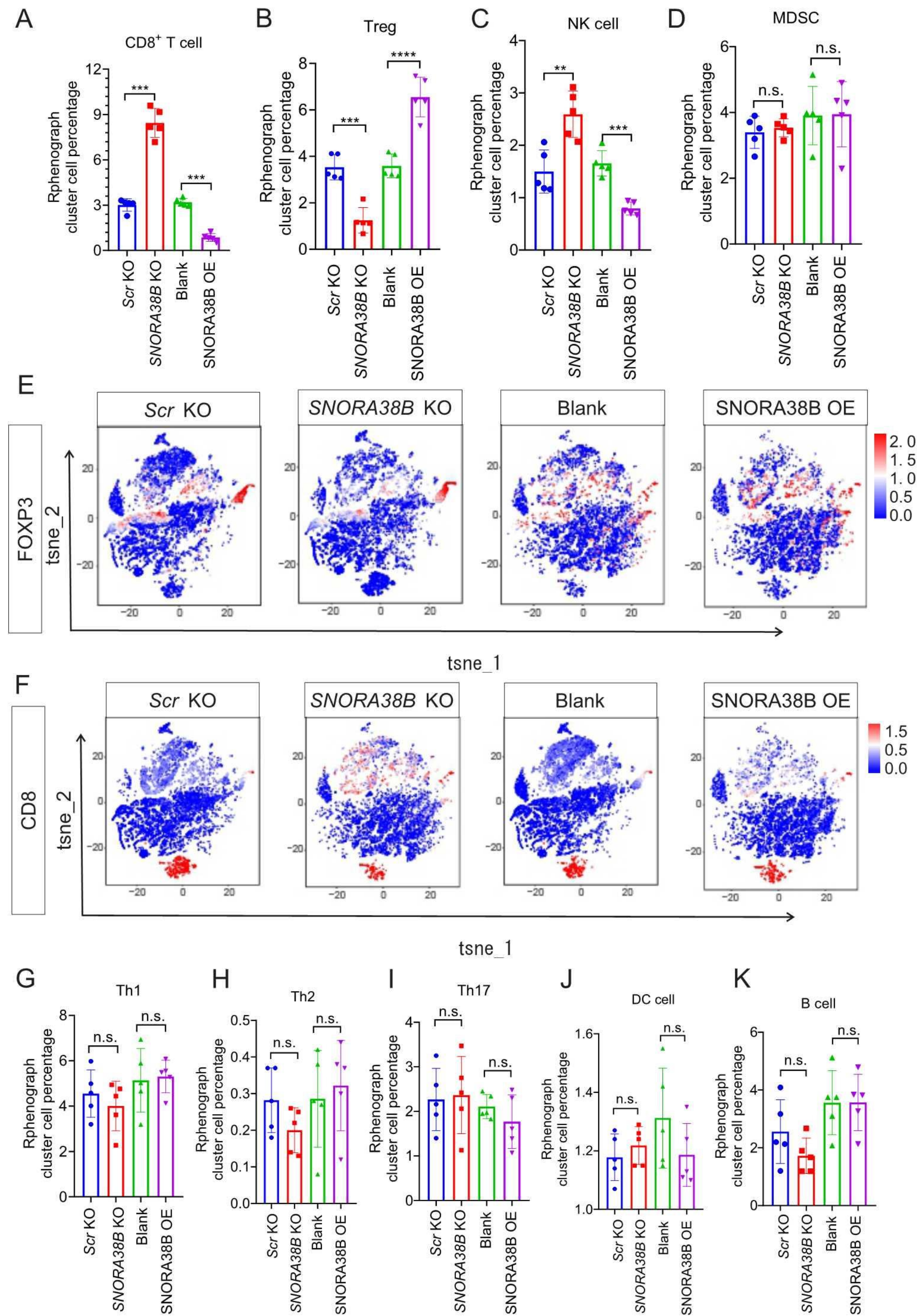
Supplemental Figure 2. SNORA38B accelerated cell proliferation, migration and invasion *in vitro*. **A.** Three kinds of siRNAs designed for SNORA38B were transfected into A549 and H1975 cells for 48h and the expression level of SNORA38B was detected by qRT-PCR. **B.** Overexpression plasmid vector designed for SNORA38B was transfected in A549 and H1975 cells for 48hrs and the expression level of SNORA38B was detected by qRT-PCR. **C-D.** Cell proliferation of *SNORA38B* KO/SNORA38B OE A549 or H1975 cells and its counterparts. Tested using EdU staining assay. Bar=50μm. **E-F.** The statistical analysis for **c**ell proliferation of *SNORA38B* KO/ SNORA38B OE A549/H1975 cells and its counterparts. Bar=50μm. **G-H.** Ki-67 positive cells detected by flow cytometry analysis. **I-M.** Migration and invasion ability of *SNORA38B* KO/ SNORA38B OE A549/H1975 cells and its counterparts using transwell migration/invasion assay. Bar=100μm. $^{**}P<0.01$, $^{***}P<0.001$, $^{****}P<0.0001$. Assays were conducted in triple. Means ± SD were shown. Statistical analysis was performed by one-way ANOVA. Comparison between groups (*SNORA38B* KO and Scr KO, SNORA38B OE and vector OE) using LSD method.

Supplementary Figure 3



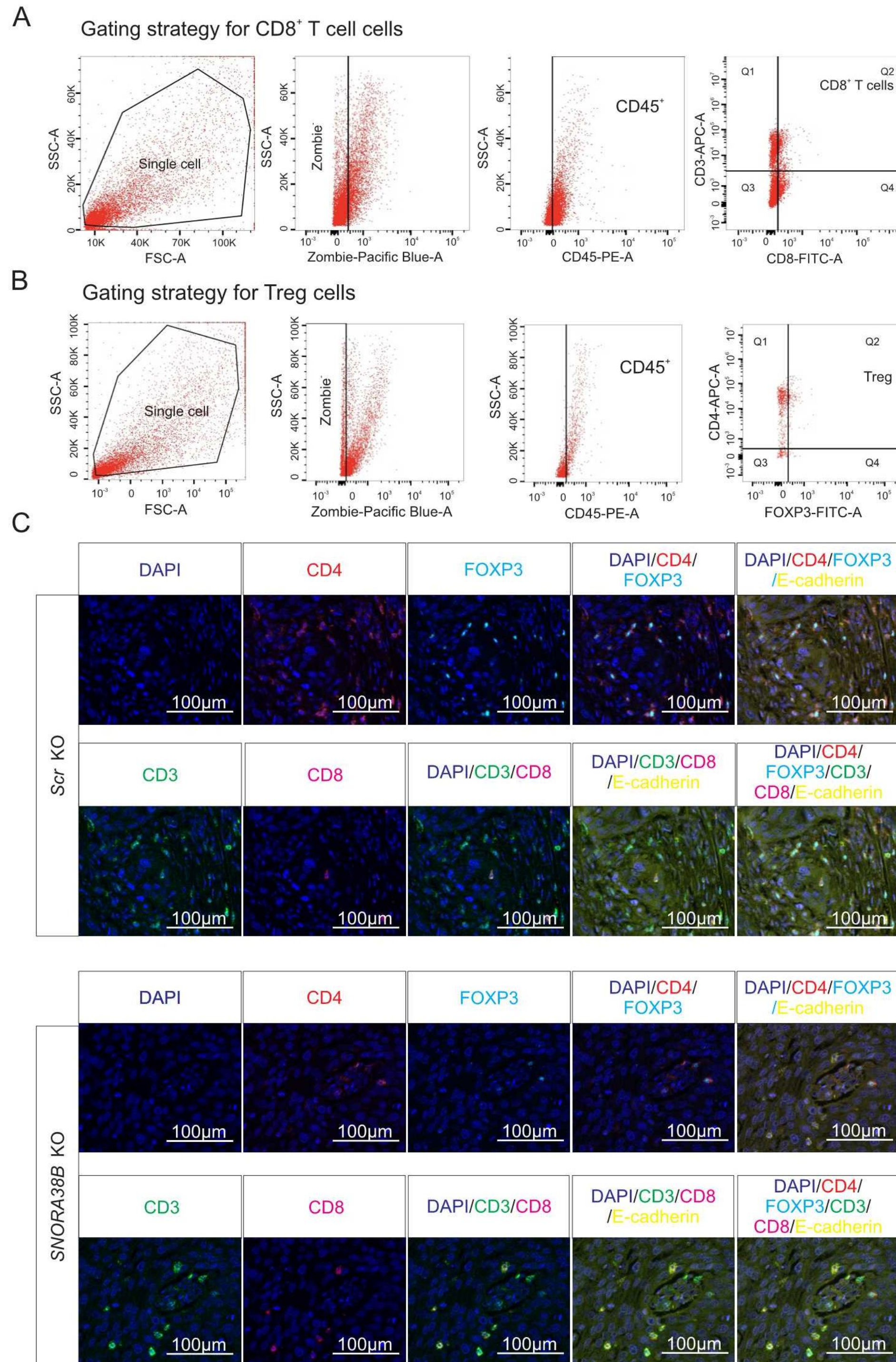
Supplemental Figure 3. SNORA38B inhibited cell apoptosis *in vitro* **A-C.** Quantification of *SNORA38B* KO/ SNORA38B OE A549/H1975 cell apoptosis using Annexin V/PI with flow cytometry. ****$P<0.0001$. Assays were conducted in triple. Means ± SD were shown. Statistical analysis was performed by one-way ANOVA. Comparison between groups (*SNORA38B* KO and Scr KO, SNORA38B OE and vector OE) using LSD method.

Supplementary Figure 4



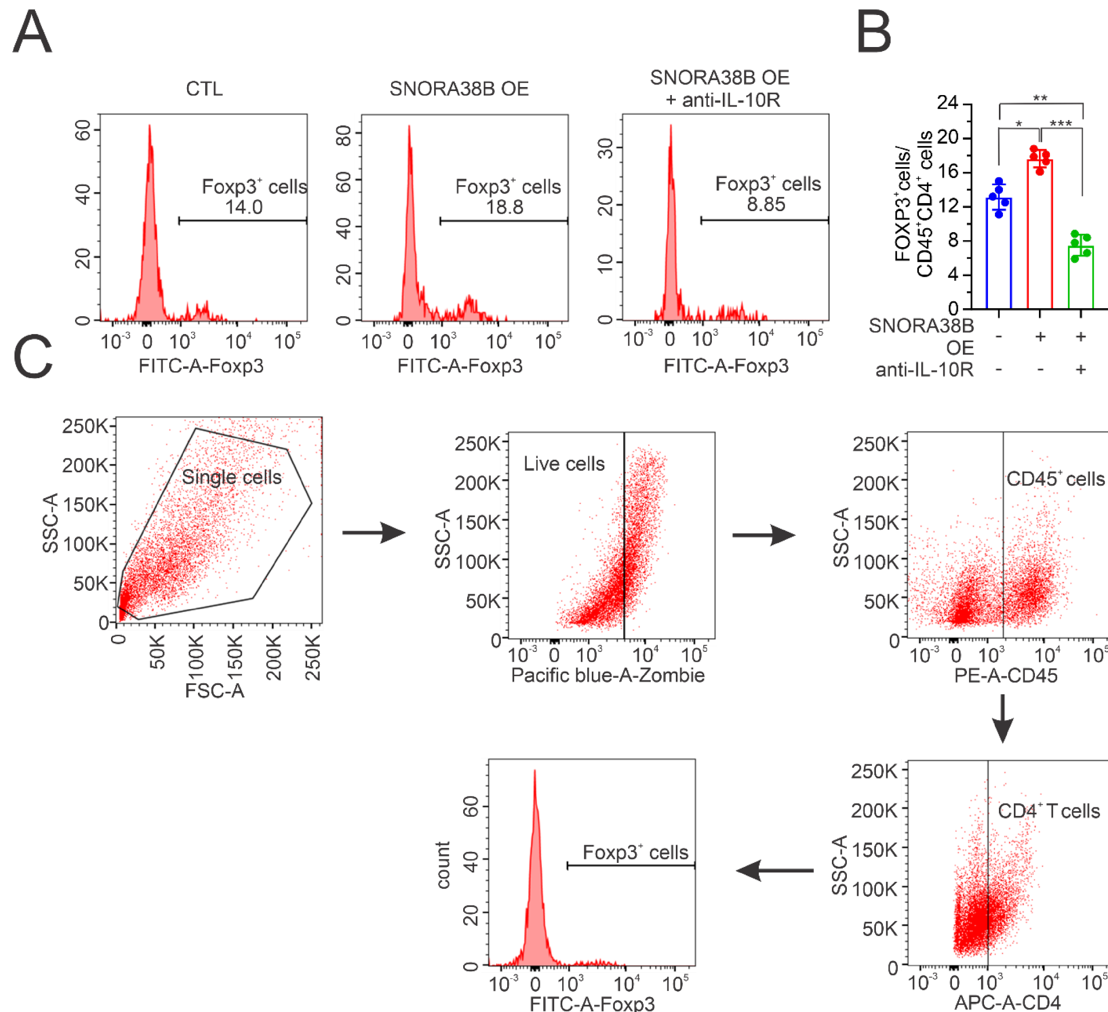
Supplemental Figure 4. SNORA38B regulated Treg infiltration in tumor isolated from C57BL/6J mice. **A-D**. Quantification of CyTOF analysis of target clusters including $CD8^+$ T cell, Treg, NK cell and MDCS. N=5 per group. **E-F**. Representing images of CyTOF analysis of FOXP3 and CD8 using RphenoGraph. **G-K.** Quantification of CyTOF analysis of target clusters including Th1, Th2, Th17, DC cell, B cell. ***$P<0.001$, ****$P<0.0001$. Means ± SD was shown. Statistical analysis was subjected to one-way ANOVA. Comparison between-group using LSD method.

Supplementary Figure 5



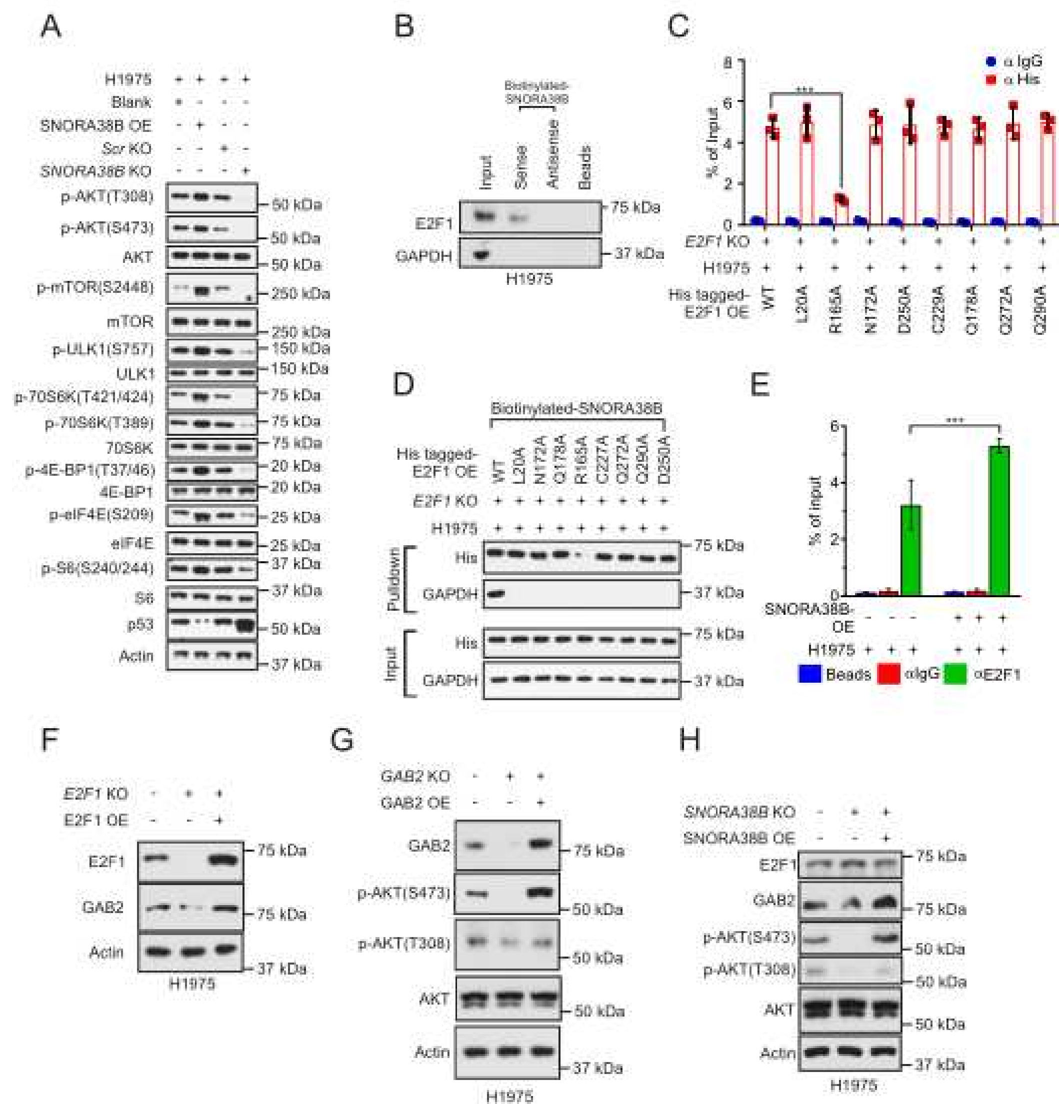
Supplemental Figure 5. SNORA38B regulated Treg infiltration in tumor isolated from C57BL/6J mice. **A-B.** Flow cytometry gating schemes for $CD3^{+}CD8^{+}$ T cells and $CD4^{+}FOXP3^{+}$ Treg were shown. Samples using single tumor cells preparation isolated from LLC injected C57BL/6J mice with *SNORA38B* KO or SNORA38B OE. $CD45^{+}$ cells (FITC positive) were assessed follow FSC and SSC methods, then cells were gated according to $CD3^{+}CD8^{+}$ or $CD4^{+}FOXP3^{+}$. Normalized using background value. **C-D.** Representative images of mIHC staining using the isolated tumor tissues from Scr KO and *SNORA38B* KO groups of C57BL/6J mice. CD4, FOXP3, CD3, CD8 and E-cadherin were shown in different colors.

Supplementary Figure 6



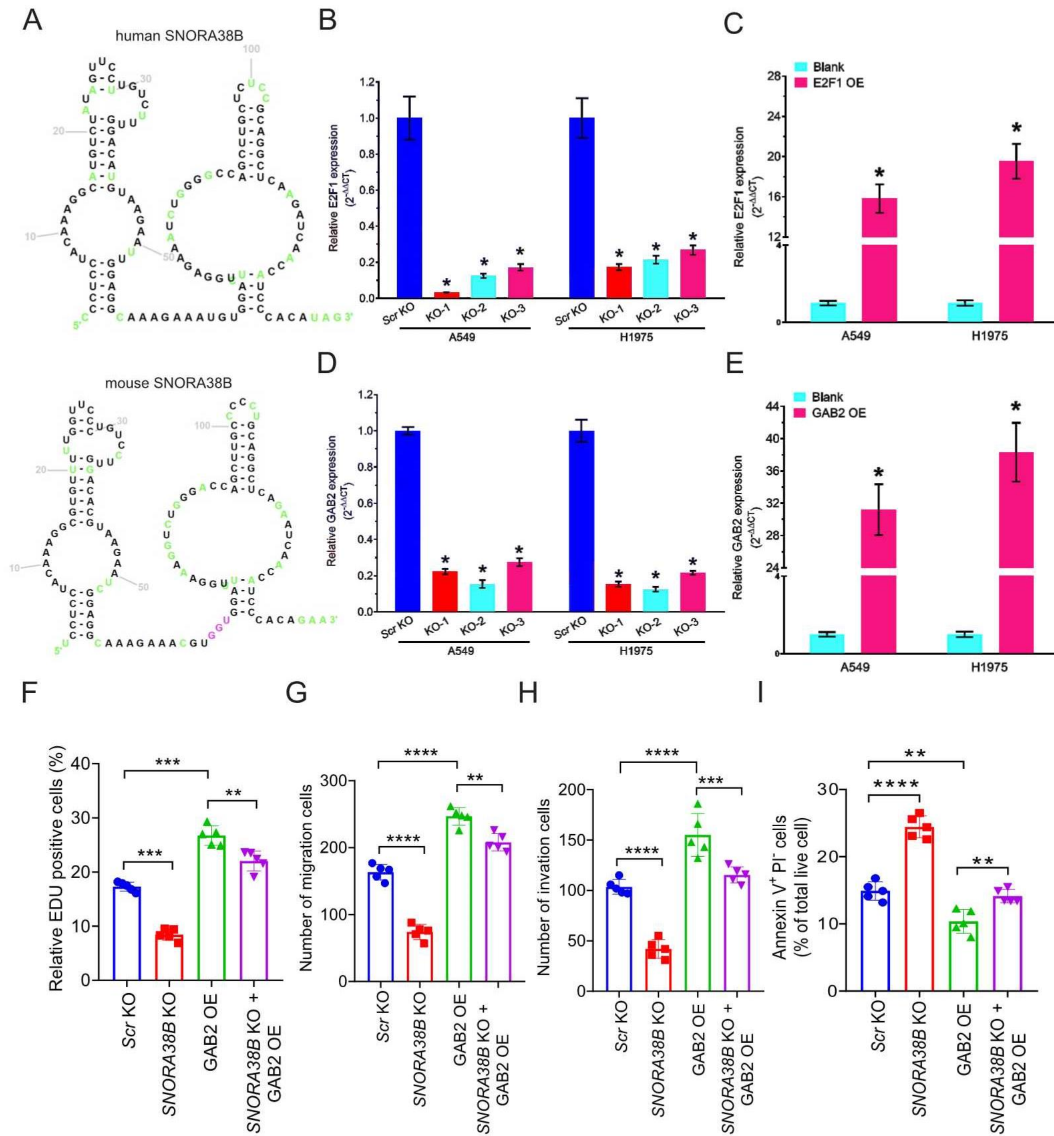
Supplemental Figure 6. SNORA38B promoted tumor progression in C57BL/6J mice and regulates Treg infiltration. **A.** Flow cytometry detection of CD4+FOXP3+ Treg infiltration in tumors isolated from C57BL/6J mice treated with vector OE, SNORA38B OE and SNORA38B OE + anti-IL-10R. n=5 per group. **B.** Proportion of CD4+FOXP3+ Treg in leukocyte. **C**. Flow cytometry gating schemes for CD4+FOXP3+ Treg were shown. CD45+ cells (PE positive) were assessed follow FSC and SSC methods, then were gated according to CD4+ and FOXP3+. Normalized using background value. $^*P<0.5$, $^{**}P<0.01$, $^{***}P<0.001$, means ±SD was shown. Statistical analysis was performed by one-way ANOVA, comparison between-group using LDS method.

Supplementary Figure 7



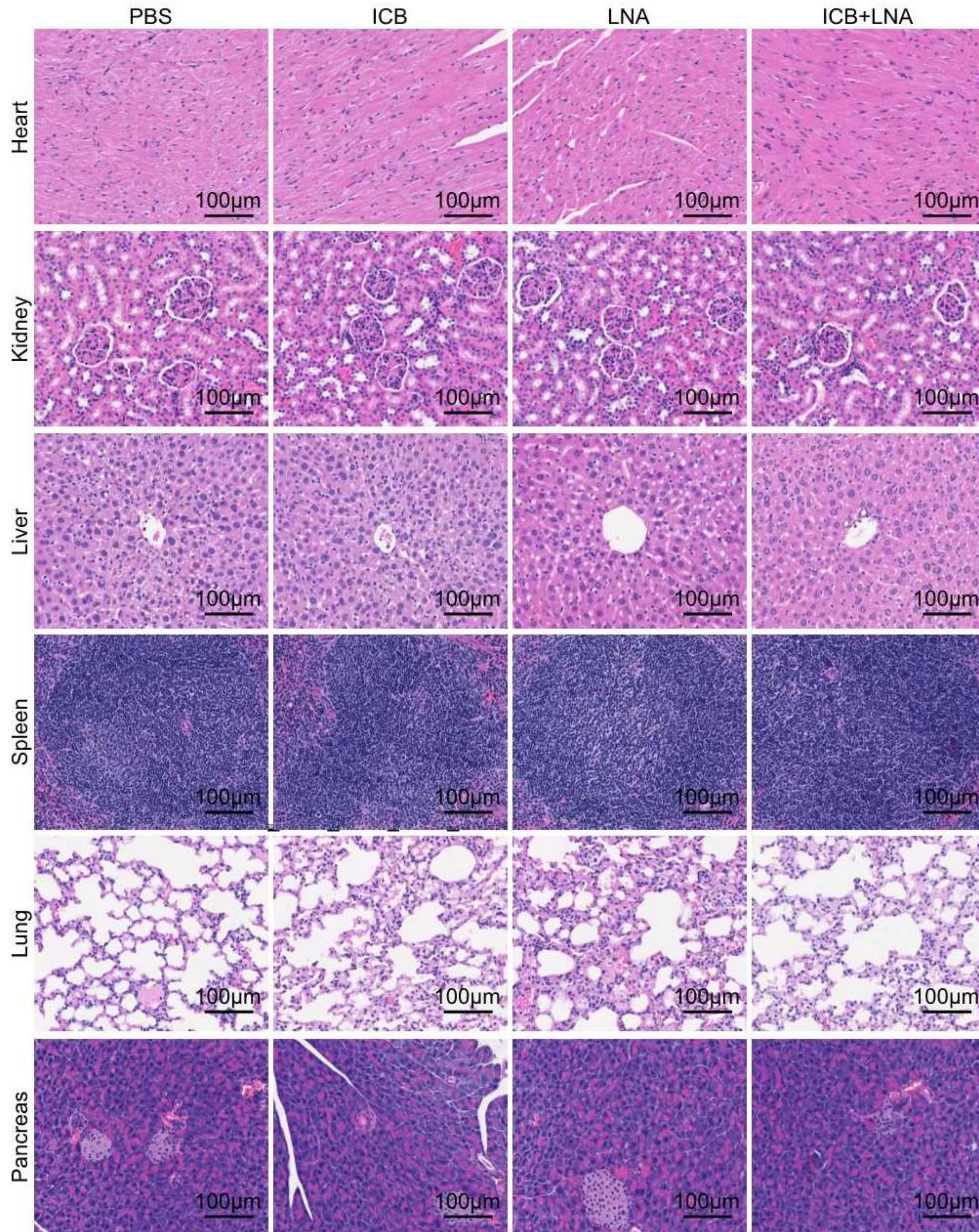
Supplemental Figure 7. SNORA38B directly bound with E2F1 and positively regulated GAB2/AKT pathway. **A.** Western blot analyses of AKT/mTOR and its downstream effectors in H1975 cells transfected with *SNORA38B* KO, SNORA38B OE and their counterparts. **B.** RNA pulldown assay detected the interaction of SONAR38B and E2F1 in H1975 cells using antisense snoRNA and beads as controls. **C.** RIP assay detected the binding activities between his-tagged E2F1-WT or -mutants with SNORA38B in E2F1-WT or -mutants treated E2F1-KO H1975 cells. **D.** RNA pulldown assay detected the interaction of SONAR38B and E2F1-WT or -mutants in E2F1 WT or mutants treated E2F1-KO H1975 cells. **E.** Binding activity between GAB2 promoter and E2F1 was shown using ChIP assay in H1975 cells. Beads and anti-IgG were utilized as controls. **F.** Western blotting assay of E2F1 and GAB2 in H1975 cells transfected with *E2F1* KO/OE. Actin was used as loading control. **G.** Western blotting assay of GAB2, AKT and p-AKT (S473 and T308) in H1975 cells transfected with *GAB2* KO/OE. Actin was used as loading control. **H.** Western blotting assay of E2F1, GAB2, AKT and p-AKT (S473 and T308) in H1975 cells transfected with *SNORA38B* KO/OE. Actin was used as loading control. ***$P < 0.001$. Means ± SD was shown. Statistical analysis was subjected to Student's *t*-test and one-way ANOVA. Assays were conducted in triple.

Supplementary Figure 8



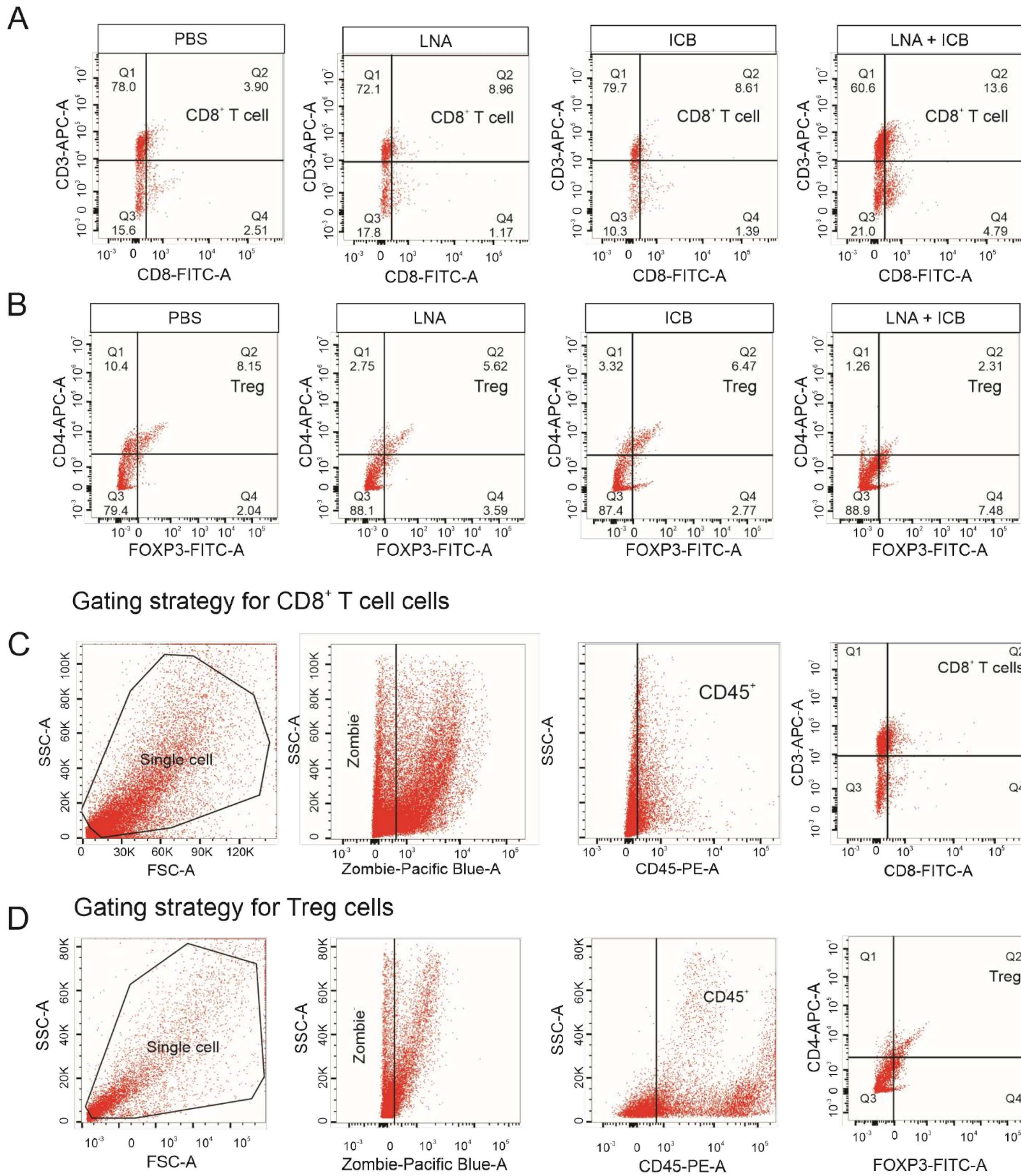
Supplemental Figure 8. SNORA38B positively regulated GAB2/AKT pathway and facilitated NSCLC cells proliferation, migration and invasion. **A.** Secondary structure of SNORA38B using the RNA Central website. **B-C.** Transfection efficiency of knockout and overexpress of E2F1 in A549 and H1975 cells. **D-E.** Transfection efficiency of knockout and overexpression of GAB2 in A549 and H1975 cells. **F**. Proliferation of H1975 cells transfected with Scr KO, *SNORA38B* KO, GAB2 OE and *SNORA38B* KO + GAB2 OE. EdU staining assay was used and the positive cells were quantified. **G-H.** Migration and invasion of H1975 cells transfected with Scr KO, *SNORA38B* KO, GAB2 OE and *SNORA38B* KO + GAB2 OE. Transwell migration and invasion assay were performed. The migrated and invaded cells were quantified. **I.** Apoptosis of H1975 cells transfected with Scr KO, *SNORA38B* KO, GAB2 OE and *SNORA38B* KO + GAB2 OE. Annexin V-FITC/PI staining was performed; apoptosis cells were quantified. $^{**}P<0.01$, $^{***}P<0.001$, $^{****}P<0.0001$. Assays were conducted in triple. Means ± SD was shown. Statistical analysis was subjected to Student's t-test and one-way ANOVA, comparison between-group using LSD method.

Supplementary Figure 9



Supplemental Figure 9. Evaluation of the potential toxicity for the combinatorial treatment using LNA and ICB. H&E staining for heart, kidney, liver, lung, spleen and pancreas of PBS, LNA, ICB and LNA+ICB treated mice. Scale bars, 100 µm.

Supplementary Figure 10



Supplemental Figure 10. SNORA38B LNAs sensitized NSCLC to ICBs treatment**. A-B.** Flow cytometry detection of $CD3^{+}CD8^{+}$ T cells and $CD4^{+}FOXP3^{+}$ Treg isolated from LLC cells injected C57BL/6J mice treated with PBS, LNA, ICB and LNA+ICB. **C-D.** Flow cytometry gating schemes for $CD3^{+}CD8^{+}$ T cells and $CD4^{+}FOXP3^{+}$ Treg were shown. Samples using single tumor cells preparation isolated from C57BL/6J mice treated with PBS, LNA, ICB and LNA+ICB. $CD45^{+}$ cells (PE positive) were assessed follow FSC and SSC methods, then were gated according to $CD3^{+}CD8^{+}$ or $CD4^{+}FOXP3^{+}$. Normalized using background value.