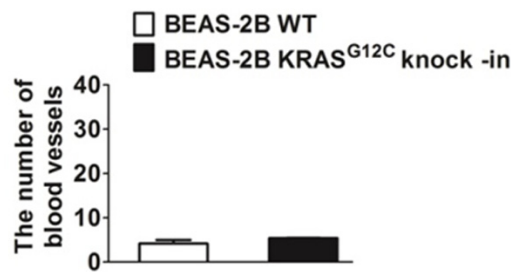
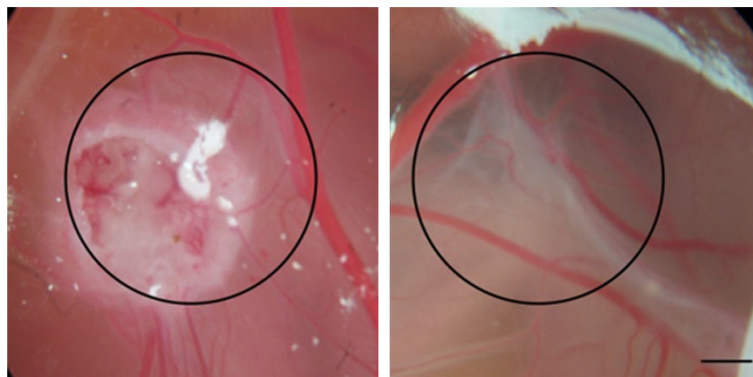


## Targeting NRAS<sup>Q61K</sup> mutant delays NSCLC growth

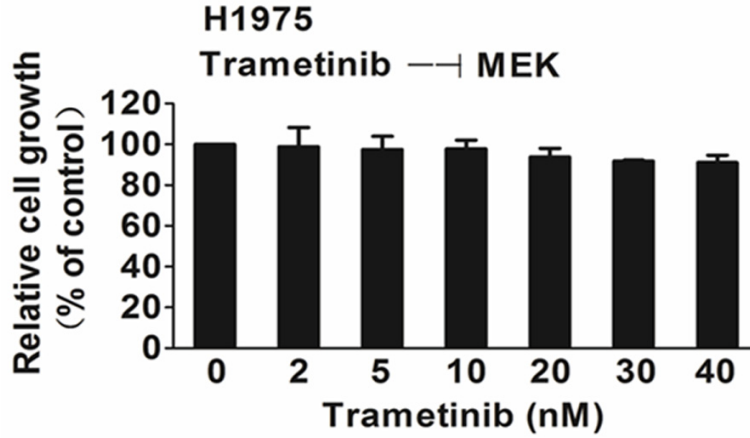
**Supplementary Table 1.** Primers used for PCR and sequence analysis

VEGFA	Forward: 5'-GCTCCTGGAAGCCATTGAGAA-3' Reverse: 5'-GTCGATCATCTCCAAGTCCAC-3'
IL-6	Forward: 5'-GTGGCCAAGG ACGAGGTG-3' Reverse: 5'-ACAGGTGGAAGAACAGCTCGC-3'
PDGFA	Forward: 5'-GGCTCATGCCTTCGCCCCAG-3' Reverse: 5'-ACTCCCATCGGCGTTCCCA-3'
FGF1	Forward: 5'-TGACAGCGACAAGAAGTG-3' Reverse: 5'-CAGTGAAGCGGTACATAGG-3'
CCL2	Forward: 5'-TCAACTCAAGCTCCTAA-3' Reverse: 5'-CCACTCAGACTTTATTCAA-3'
VEGFC	Forward: 5'-TCACAGGCTTCCATTGACCAG-3' Reverse: 5'-CCGAGGCTTTTCTACCAGA-3'
IL-8	Forward: 5'-TGCTGGAGAACATTCTAGAGAAC-3' Reverse: 5'-CACAGTCTCTGAAGGTGGTTT-3'
CXCL2	Forward: 5'-ACCATGCCGCCCTCCGGG-3' Reverse: 5'-TCAGCTGCACTTGCAGGAGC-3'
$\beta$ -actin	Forward: 5'-GCTGCGTGTGGCCCTGAG-3' Reverse: 5'-ACGCAGGATGGCATGAGGGA-3'

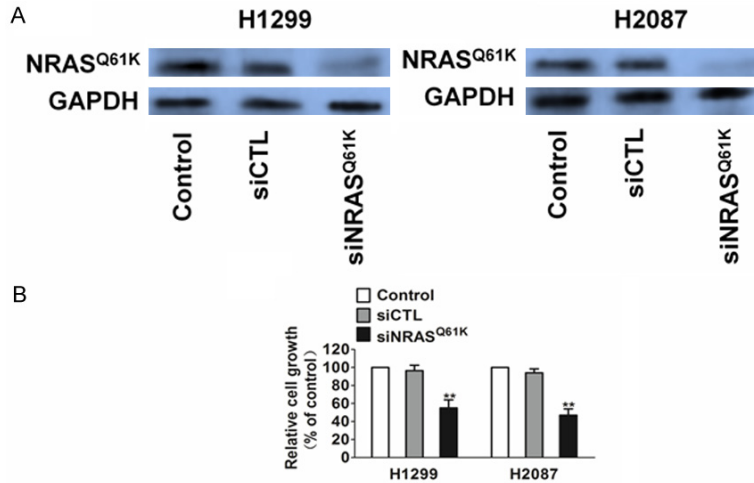


**Supplementary Figure 1.** The effect of KRAS<sup>G12C</sup> on BEAS-2B cells angiogenesis. Representative images of BEAS-2B cells plated on the CAM. Scale bar: 1 cm. Qualitative assessment of angiogenesis in the CAM assay. Data are from three independent experiments and are mean  $\pm$  SD. n = 6.

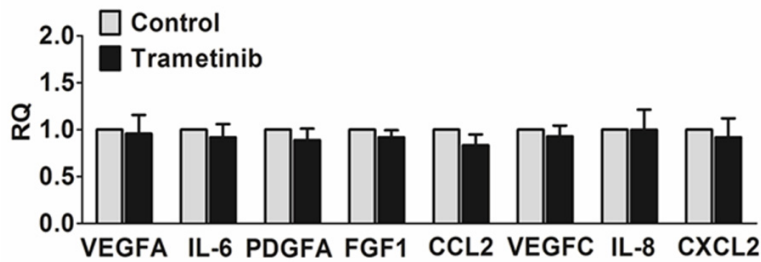
Targeting NRAS<sup>Q61K</sup> mutant delays NSCLC growth



**Supplementary Figure 2.** Trametinib has no effect on wild type NRAS NSCLC H1975 cells growth. Proliferation of H1975 harboring wild type NRAS was assessed with increased trametinib concentration. Data are expressed as percentage of viability compared with vehicle by the MTT assay. Mean  $\pm$  SD of three independent experiments performed.



**Supplementary Figure 3.** Tumor cells were transfected with NRAS<sup>Q61K</sup> siRNA (0.5  $\mu$ g/well for 96 well culture plates and 3  $\mu$ g/well for 6 well culture plates). A. Western blot analysis to assay the NRAS<sup>Q61K</sup> in control cells, siCTL and siNRAS<sup>Q61K</sup> transfected cells. GAPDH was used as a loading control. B. Proliferation assays indicated that NRAS<sup>Q61K</sup> siRNA exerted inhibition on both H1299 and H2087 cells proliferation in vitro. Data are from three independent experiments and are mean  $\pm$  SD. n = 3, \*\**P* < 0.01 compared with control.



**Supplementary Figure 4.** Trametinib treatment regulates the expression of pro-angiogenic factors. Expression of proangiogenic factors was evaluated by real-time PCR. H1975 cells carrying wild type NRAS was treated for 24 h with trametinib. Data are expressed as relative quantity (RQ) of trametinib compared with vehicle-treated samples. Bars show mean  $\pm$  SD of triplicate measurements.