Supplementary Information

Adaptive and acquired resistance to EGFR inhibitors converge on the MAPK pathway

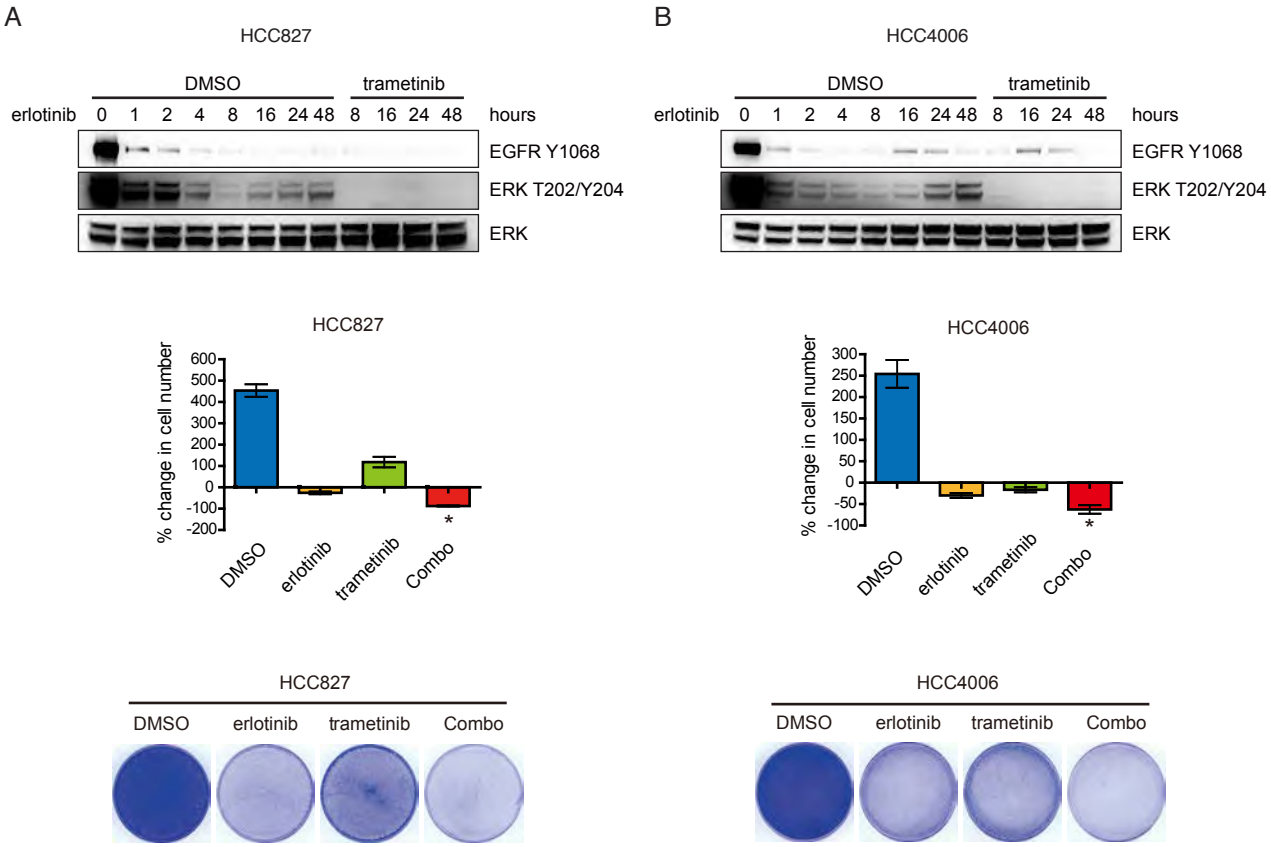
Pengfei Ma[1, *], Yujie Fu[2, *], Minjiang Chen[3, *], Ying Jing[1], Jie Wu[4], Ke Li[5], Ying Shen[6, 7], Jian-Xin Gao[1], Mengzhao Wang[3], Xiaojing Zhao[2, #], Guanglei Zhuang[1, #]

[1]State Key Laboratory of Oncogenes and Related Genes, Renji-Med X Clinical Stem Cell Research Center, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
[2]Department of thoracic surgery, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
[3]Department of Respiratory Medicine, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China
[4]Department of Pathology, the affiliated hospital of Qingdao University, Qingdao, China
[5]Bio-X Institute, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders, Ministry of Education, Shanghai Jiao Tong University, Shanghai, China
[6]Department of Pharmacology and Chemical Biology, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[7]Shanghai Collaborative Innovation Center for Translational Medicine, Shanghai, China

[#]Corresponding authors:
Guanglei Zhuang
State Key Laboratory of Oncogenes and Related Genes, Renji-Med X Clinical Stem Cell Research Center, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
Email: zhuangguanglei@gmail.com
or
Xiaojing Zhao
Department of thoracic surgery, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
Email: zhaoxiaojing@renji.com

[*]These authors contributed equally to this work.

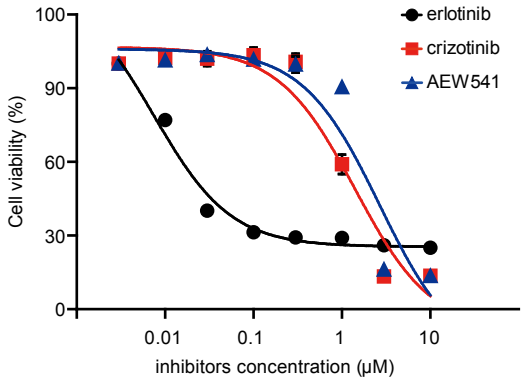
Supplementary Figure 1.



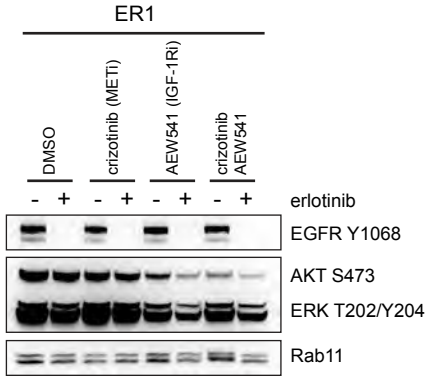
Supplementary Figure 1. A. Upper panel: Feedback activation of phospho-ERK in HCC827 cells; Middle panel: Cell viability assay of HCC827 cells treated with erlotinib (1 μM), trametinb (0.5 μM) or combination (Combo). *P<0.05, ANOVA followed by Tukey's post-test; Bottom panel: HCC827 cells were treated for 10 days as indicated and the cells were stained with crystal violet. B. Upper panel: Feedback activation of phospho-ERK in HCC4006 cells; Middle panel: Cell viability assay of HCC4006 cells treated with erlotinib (1 μM), trametinb (0.5 μM) or combination (Combo). *P<0.05, ANOVA followed by Tukey's post-test; Bottom panel: HCC4006 cells were treated for 10 days as indicated and the cells were stained with crystal violet.

Supplementary Figure 2.

A

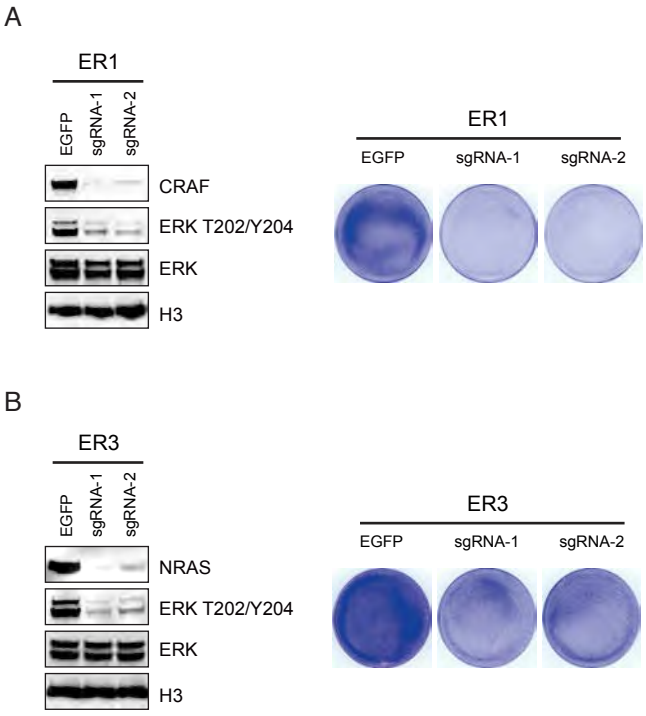


B



Supplementary Figure 2. A. Cell viability of PC9 cells treated various concentrations of erlotinib (1 μM), crizotinib (0.5 μM) or AEW541 (0.5 μM). B. Effects of erlotinib and inhibitors of MET or IGF-1R on phosphorylation of AKT and ERK in ER1 cells.

Supplementary Figure 3.



Supplementary Figure 3. A. CRAF CRISPR-Cas9 knockout and crystal violet staining of ER1 cells. B. NRAS CRISPR-Cas9 knockout and crystal violet staining of ER3 cells.