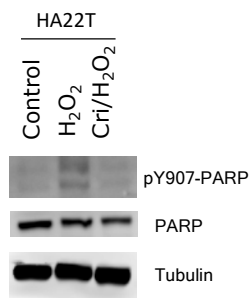
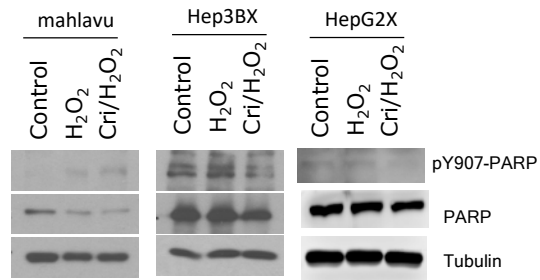


Supplementary Information

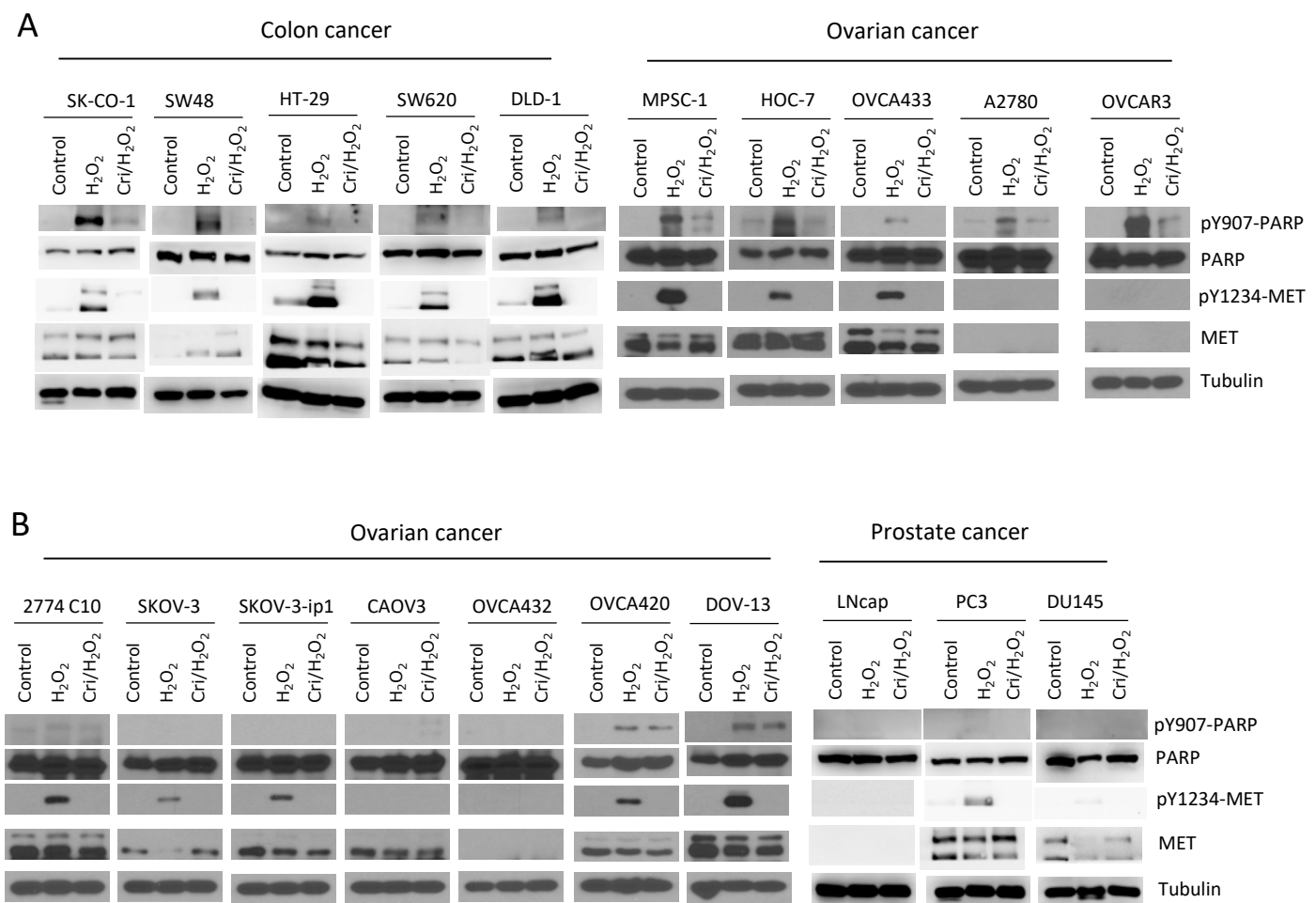
Supplementary Table S1. Clinicopathological characteristics of HCC Patients (n= 274)

Characteristics	Case number	%
Sex		
Female	53	19.3
Male	221	80.7
Age (years)		
≤ 51	137	50.0
> 51	137	50.0
HBsAg		
Negative	8	2.9
Positive	266	97.1
Cirrhosis		
No	23	8.4
Yes	251	91.6
ALT (U/L)		
≤75	243	88.7
>75	31	11.3
AFP (ng/mL)		
≤20	100	36.5
>20	174	63.5
Tumor size (cm)		
≤5	230	83.9
>5	44	16.1
Tumor number		
Single	268	97.8
Multiple	6	2.2
Tumor capsule		
None	143	52.2
Complete	131	47.8
Tumor thrombus		
No	191	69.7
Yes	83	30.3
Tumor differentiation		
I-II	205	74.8
>II	69	25.2
BCLC stage		
0 /A	201	73.4
B/C	73	26.6

HBsAg, hepatitis B surface antigen; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; BCLC stage: Barcelona Clinic Liver Cancer stage.

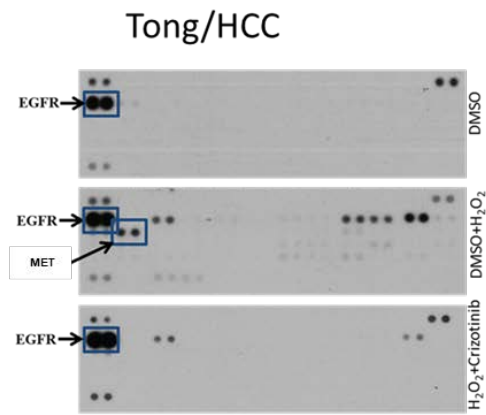
A**B**

Supplementary Figure S1. Liver cancer cell lines were treated or untreated with 1 μ M Crizotinib (Cri) for 1 h and further cultured in the presence of 20 mM H₂O₂ for additional 30 min. Cells were then lysed and subjected to Western blotting analysis with the indicated antibodies. (A) Cell line responded to Crizotinib. (B) Cell lines did not respond to Crizotinib.

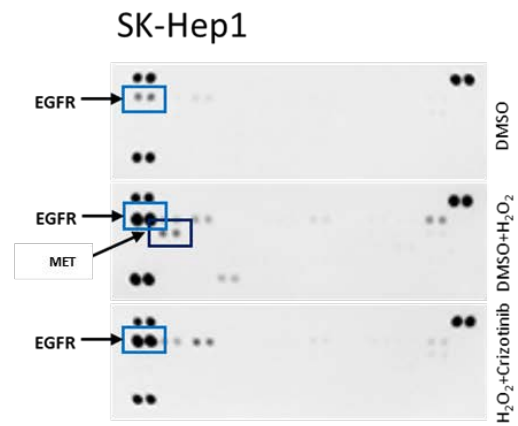


Supplementary Figure S2. Different type cancer cell lines were treated or untreated with 1 μ M Crizotinib (Cri) for 1 h and further cultured in the presence of 20 mM H₂O₂ for additional 30 min. Cells were then lysed and subjected to Western blotting analysis with the indicated antibodies. (A) Cell lines responded to Crizotinib. (B) Cell lines did not respond to Crizotinib.

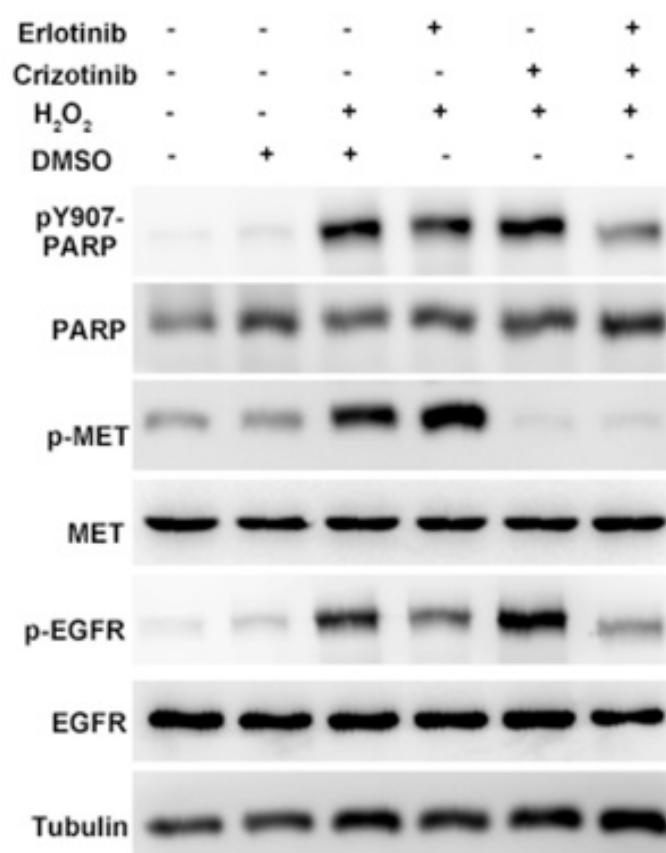
A



B



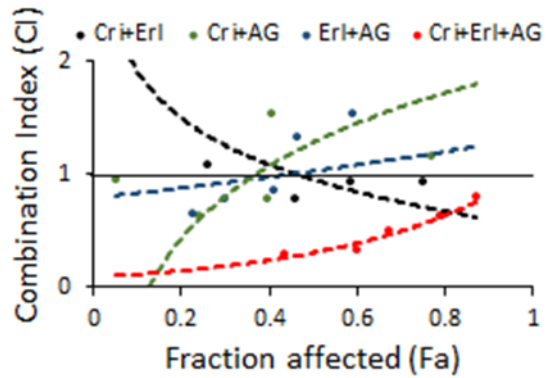
Supplementary Figure S3. Tong/HCC (A) and SK-Hep1 (B) cells were treated with 20 mM H₂O₂ with/without 1 μ M crizotinib for 30 min and subjected to RTK antibody array. The images of RTK array are shown. Summaries of these data are shown in Figure 2A and 2B.



Supplementary Figure S4. Tong cells were treated with H₂O₂ with/without 1 μ M crizotinib (METi) and/or erlotinib (EGFRi) for 30 min and subjected to Western blotting analysis with the indicated antibodies.

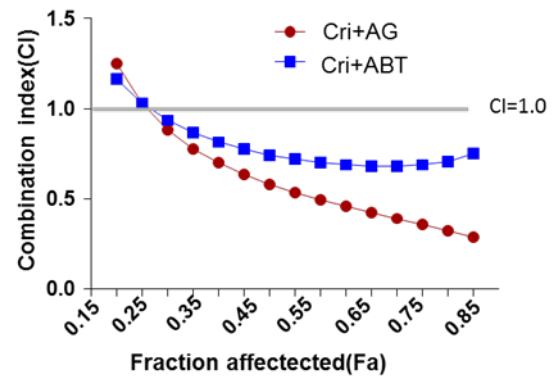
A

Hep3B

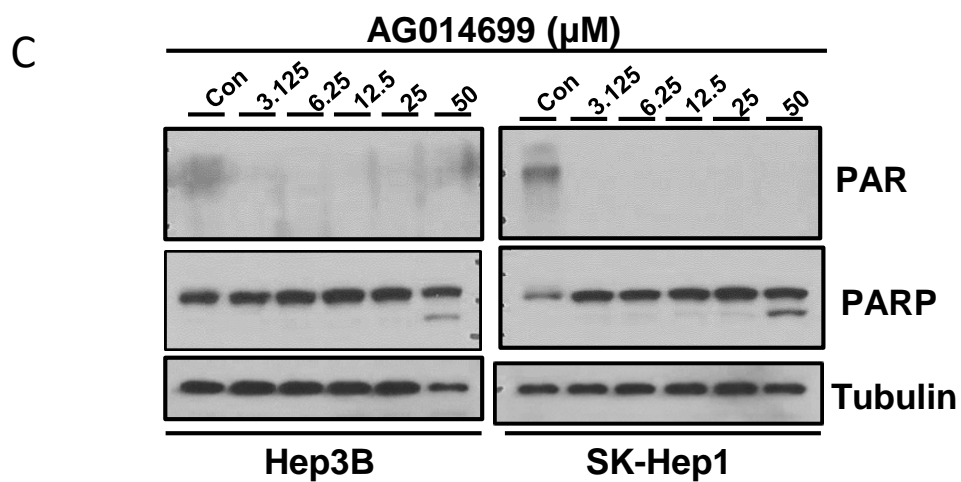
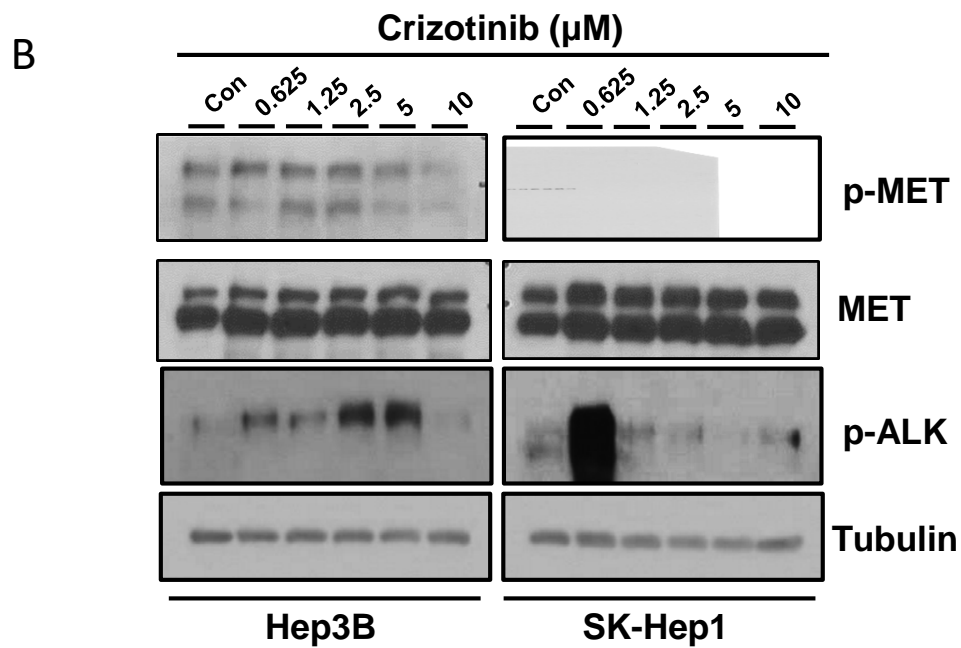
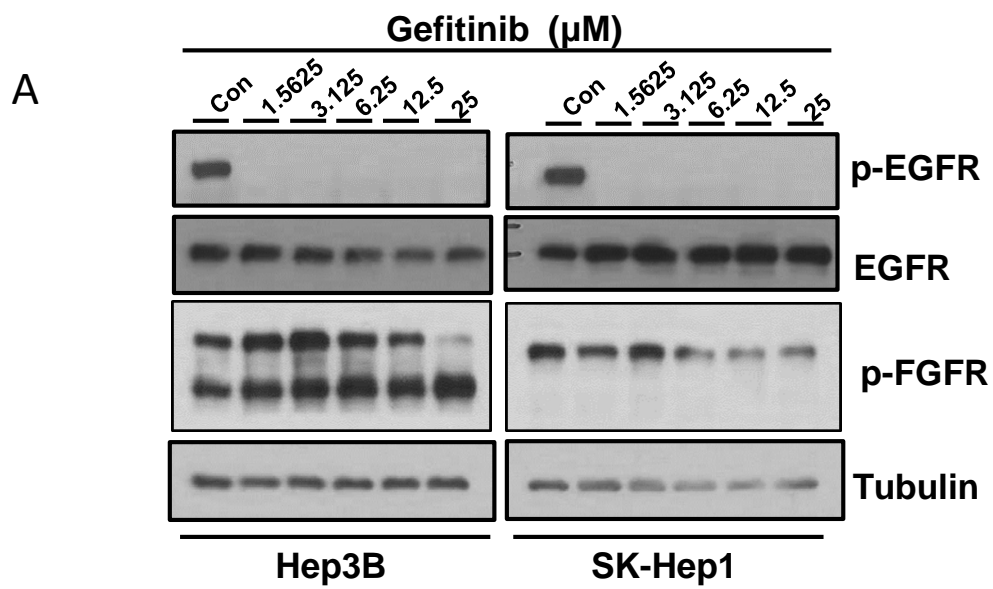


B

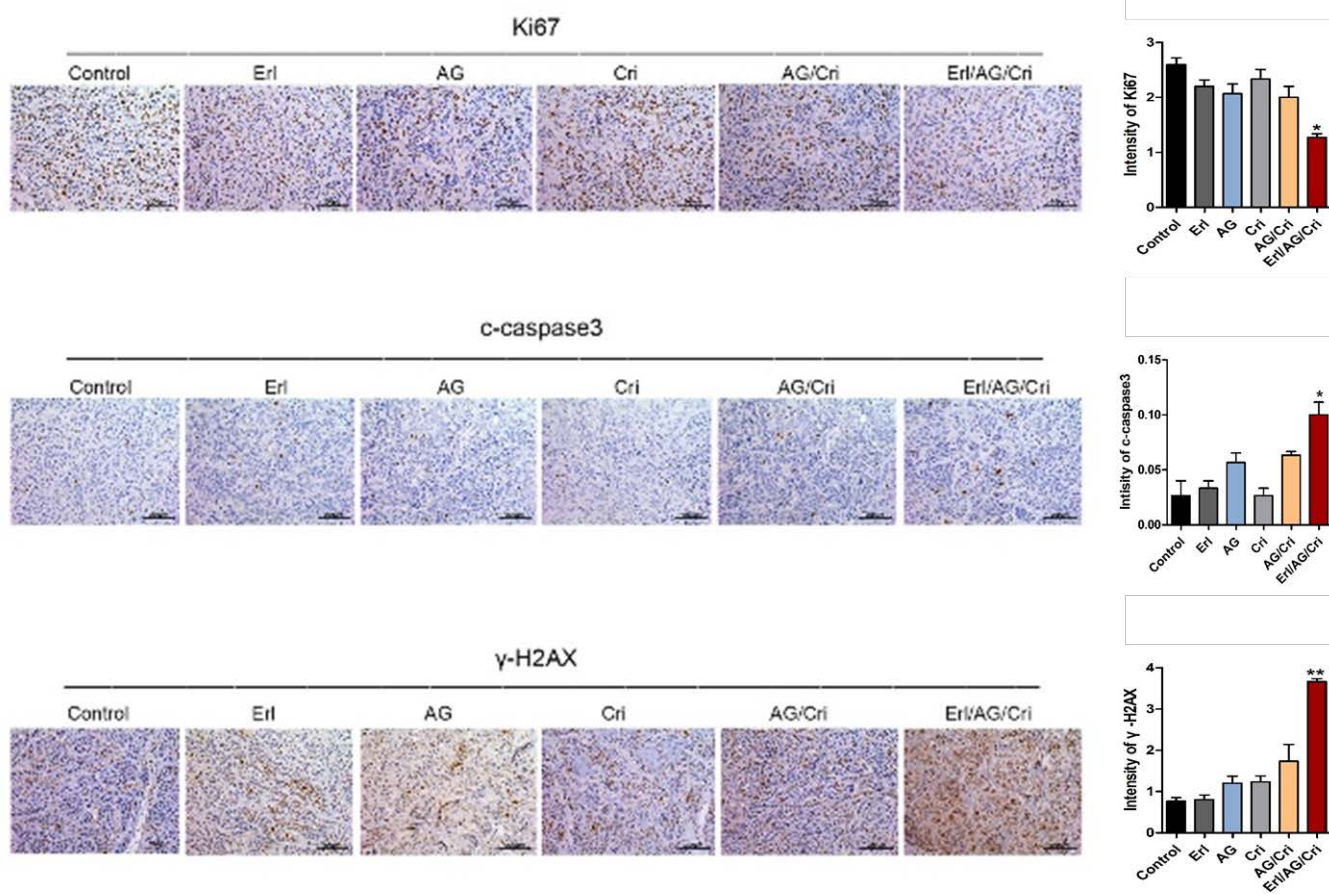
PLC/PRF5



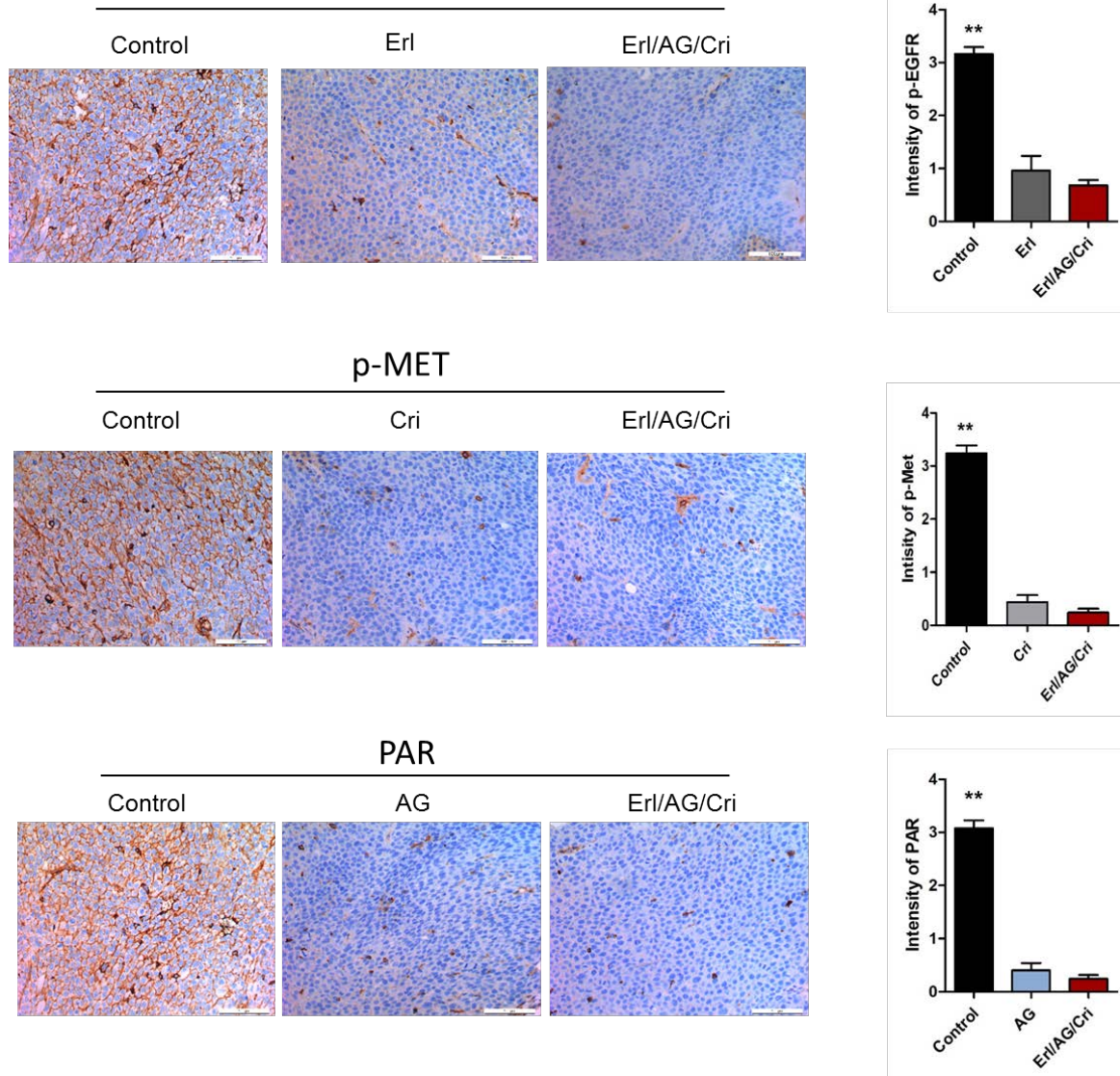
Supplementary Figure S5. (A) Hep3B cells were treated with triple inhibitors (Cri: MET inhibitor, Erl: EGFR inhibitor, AG: PARP inhibitor) for three days followed by MTT assay. The three drug combination showed the significant synergistic effect ($CI < 1$). (B) PLC/PRF5 cells were treated with the combination with MET inhibitor (Cri) and PARP inhibitors (AG or ABT) for three days, followed by MTT assay. The combinations showed synergistic effects ($CI < 1$).



Supplementary Figure S6. Hep3B and SK-Hep1 cells were treated with the indicated concentration of Gefitinib (A), Crizotinib (B) and AG014699 (C) and subjected to Western blotting analysis with the indicated antibodies.



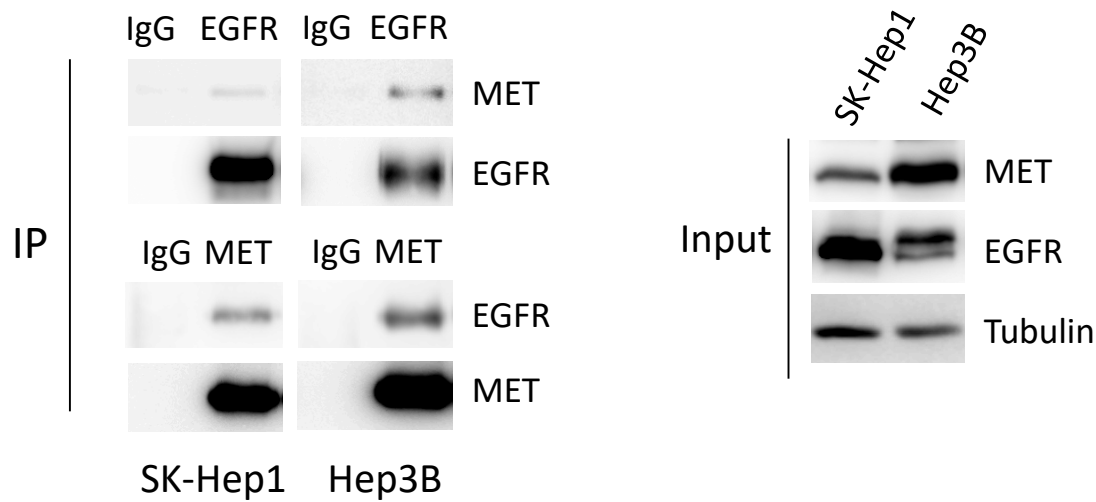
Supplementary Figure S7. Tumor tissues were subjected to IHC staining with the indicated antibodies. Ki67, cleaved caspase-3, and γ -H2AX served as markers for cell proliferation, apoptosis, and DNA damage, respectively. Representative images are shown. When Hep3B cells xenograft tumor volume reached approximately 100 mm³, the mice were then treated with the inhibitors against EGFR (Erl, Erlotinib), MET (Cri, crizotinib), PARP (AG, AG014699), or their combination. * $P < 0.05$, ** $P < 0.01$.



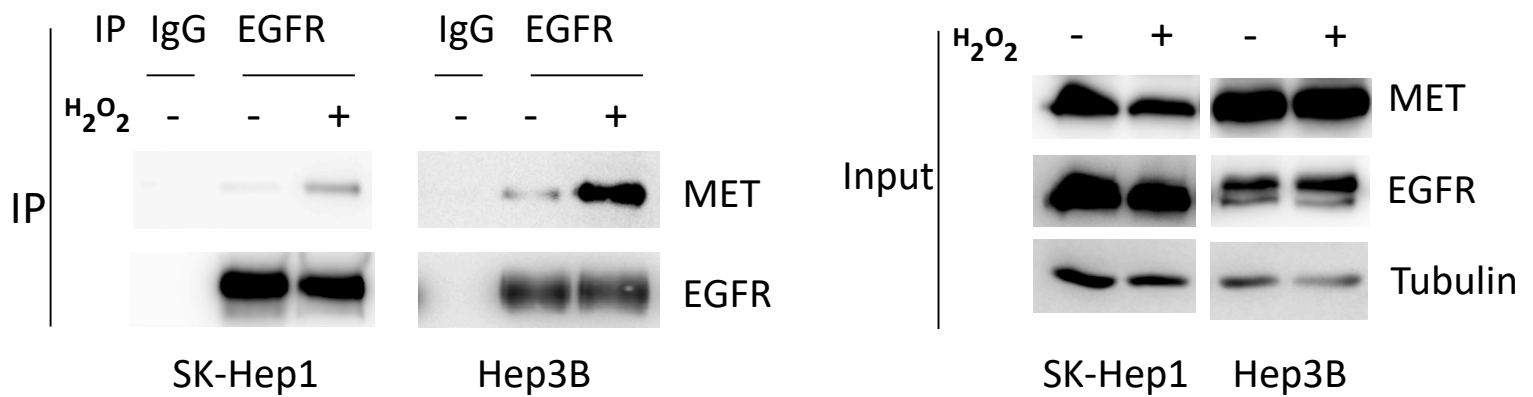
Supplementary Figure S8. In Hep3B xenograft tumor models, tumor tissues were subjected to IHC staining with the indicated antibodies after the indicated treatment. Representative images are shown.

**** $P < 0.01$.**

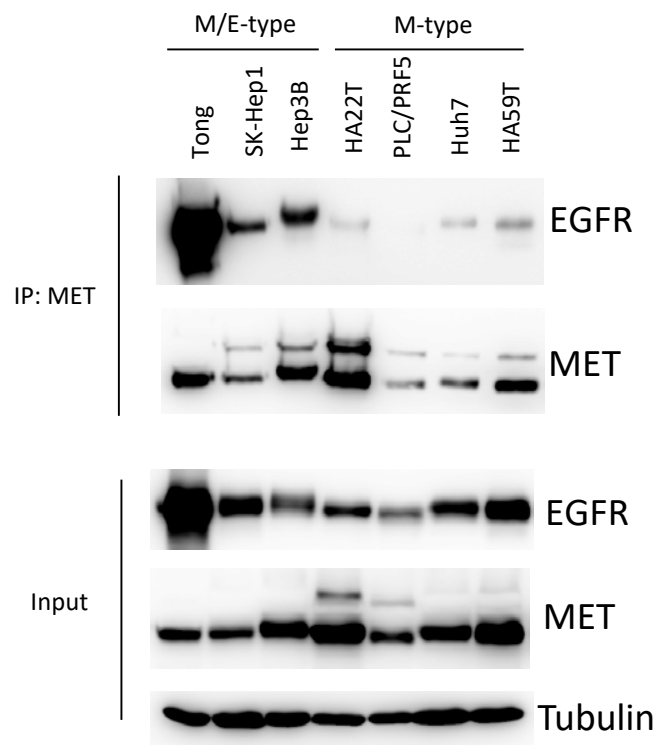
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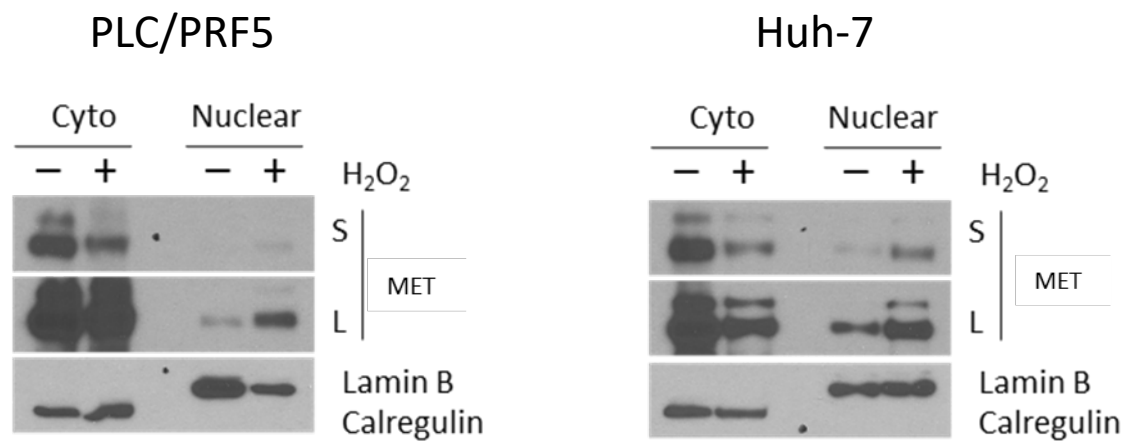
B



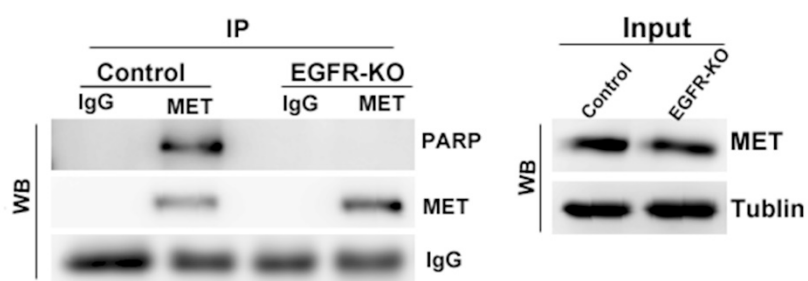
Supplementary Figure S9. (A) The interaction between MET and EGFR was determined by co-immunoprecipitation. Cell lysates from SK-Hep1 and Hep3B cells were subjected to immunoprecipitation with EGFR and MET antibody or control IgG followed by Western blotting analysis with the indicated antibodies. (B) Cell lysates from SK-Hep1 and Hep3B cells, treated with/without H_2O_2 , were subjected to immunoprecipitation with EGFR antibody or control IgG followed by Western blotting analysis with the indicated antibodies.



Supplementary Figure S10. The interaction between MET and EGFR was determined by co-immunoprecipitation in M/E-type and M-type HCC cell lines. Cell lysates from M/E-type and M-type cell lines were subjected to immunoprecipitation with MET antibody followed by Western blotting analysis with the indicated antibodies.

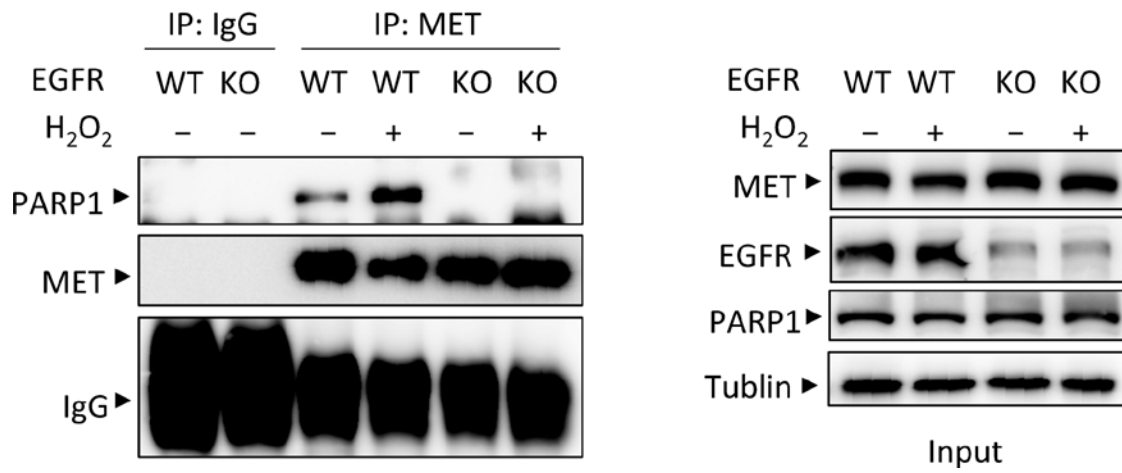


Supplementary Figure S11. ROS induced nuclear translocation of MET in PLC/PRF/5 and Huh-7. PLC/PRF/5 and Huh-7 cells were treated with or without 20 mM H_2O_2 for 30 min and then subjected to subcellular fractionation followed by Western blotting analysis with the indicated antibodies. Lamine B, nuclear marker; calregulin, cytoplasmic marker.



Supplementary Figure S12. Interaction of MET/PARP affected by EGFR in Hep3B cell line. Hep3B control and EGFR-Knockout (EGFR-KO) cells were treated with 20 mM H₂O₂ for 30 min and then subjected to immunoprecipitation with MET antibody followed by Western blotting analysis with the indicated antibodies.

SK-Hep1



Supplementary Figure S13. EGFR is required for interaction between MET and PARP in SK-HEP1 cells. SK-Hep1 control (WT) and EGFR-Knockout (KO) cells were treated with 20 mM H₂O₂ for 30 min and then subjected to immunoprecipitation with MET antibody followed by Western blotting analysis with the indicated antibodies.