А

<u>HuH7</u>



Figure S1. In vitro antiproliferative activity of lenvatinib in Hepatocellular carcinoma cell (HCC) lines.

Lenvatinib inhibited the proliferation of HuH7 (A) and Hep3B (B) cells with IC₅₀ values of 0.76 and 0.34 μ M, respectively.

Inhibition of HCC cell proliferation by lenvatinib in HuH7 (A) and Hep3B (B).

В



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Α



Figure S2. Lenvatinib and Liproxstatin. The anti-tumor effect of Lenvatinib (0.4μ M) was diminished by Liproxstatin (1μ M) in Hep3B (A) and HuH7 (B).

В



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Α



Figure S3. The caspase-3/7 activity and Lenvatinib.

The caspase-3/7 activity did not change in HuH7 (A) and Hep3B (B) cells treated with lenvatinib (HuH7: 0.8μ M Hep3B: 0.4μ M).

В



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Figure S4. Si-fibroblast growth factor receptor 4 (FGFR4) and lipid reactive oxygen species (ROS).

Si-FGFR4 increased lipid ROS accumulation in PLC.

А



Figure S5. Effect of si-fibroblast growth factor receptor 4 (FGFR4) in hepatocellular carcinoma cell line.

Si-FGFR4 increased lipid reactive oxygen species accumulation (A,B) and suppressed cell survival (C,D).

В



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Si-FGFR4 increased lipid reactive oxygen species accumulation (A,B) and suppressed cell survival (C,D).

С





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D



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Si-FGFR4 increased lipid reactive oxygen species accumulation (A,B) and suppressed cell survival (C,D).

А



Figure S6. Fibroblast growth factor receptor 4 (FGFR4) and Lenvatinib The anti-tumor effect of Lenvatinib in the absence of FGFR4 in Hep3B (A) and HuH7 (B)

В



Figure S6. Fibroblast growth factor receptor 4 (FGFR4) and Lenvatinib The anti-tumor effect of Lenvatinib in the absence of FGFR4 in Hep3B (A) and HuH7 (B)



Figure S7. Immunohistochemical staining of Fibroblast growth factor receptor 4 (FGFR4). Staining for FGFR4 with positive (A), negative (B).



Figure S8. The correlation between sensitivity to lenvatinib and P-Nrf2 expression in patients with hepatocellular carcinoma.

Immunohistochemical staining of P-Nrf2. Staining for P-Nrf2 with positive (A), negative (B).

- (C) Correlation between P-Nrf2 expression and sensitivity to lenvatinib.
- (D) Progression-free survival in patients with P-Nrf2-positive and P-Nrf2-negative lesions.



Nrf2

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Progression-free survival months

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