

NSD2 mediates NF-κB and matrix metalloproteinases to drive hepatocellular carcinoma malignant progression

Meng Xiong^{1#}, Qianshan Ding^{2,3#}, Yingjie Wu⁴, Muhammad Jamal⁵, Xingrui Zeng⁵, Yufei Lei⁵, Hengjing He⁵, Di Xiao⁵, Qiuping Zhang⁵, Liang Shao^{6*}, Xiaoxing Huang^{7*}, Xinran Li^{8,9*}

¹ School of Physical Education, Hubei Engineering University, Xiaogan, China; ² School of Medicine, Northwest University, Xi'an, China; ³ Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, China; ⁴ Department of Pathology, Zhongnan Hospital of Wuhan University, Wuhan, China; ⁵ Department of Immunology, School of Basic Medical Sciences, Wuhan University, Wuhan, China; ⁶ Department of Hematology, Zhongnan Hospital of Wuhan University, Wuhan, China; ⁷ Department of Blood Transfusion, Zhongnan Hospital of Wuhan University, Wuhan, China; ⁸ Department of Laboratory Medicine, Zhongnan Hospital of Wuhan University, Wuhan, China; ⁹ Hubei Provincial Clinical Research Center for Molecular Diagnostics, Wuhan, China

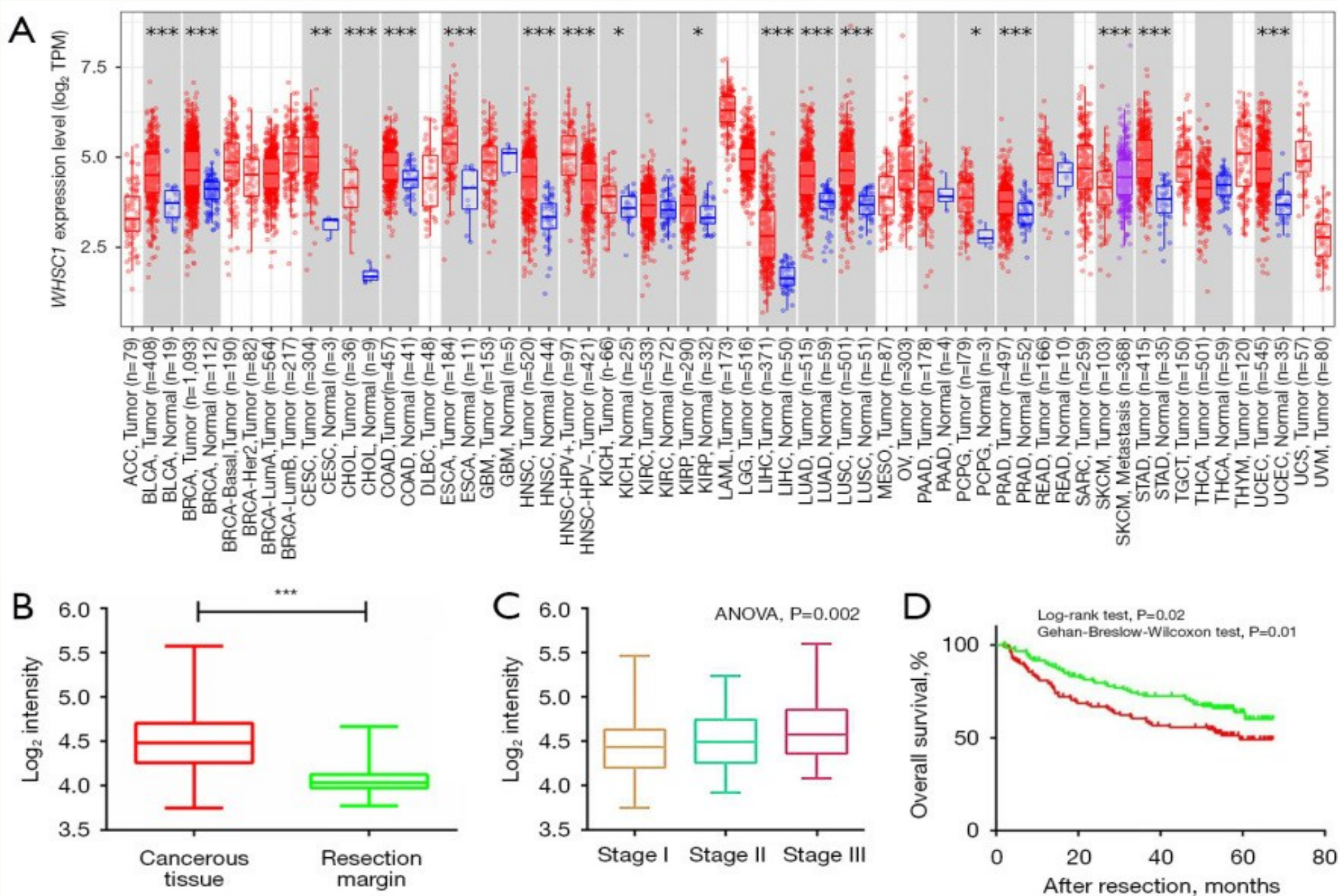
* These authors contributed equally to this work as co-first authors. # These authors contributed equally to this work.

Introduction - Aim

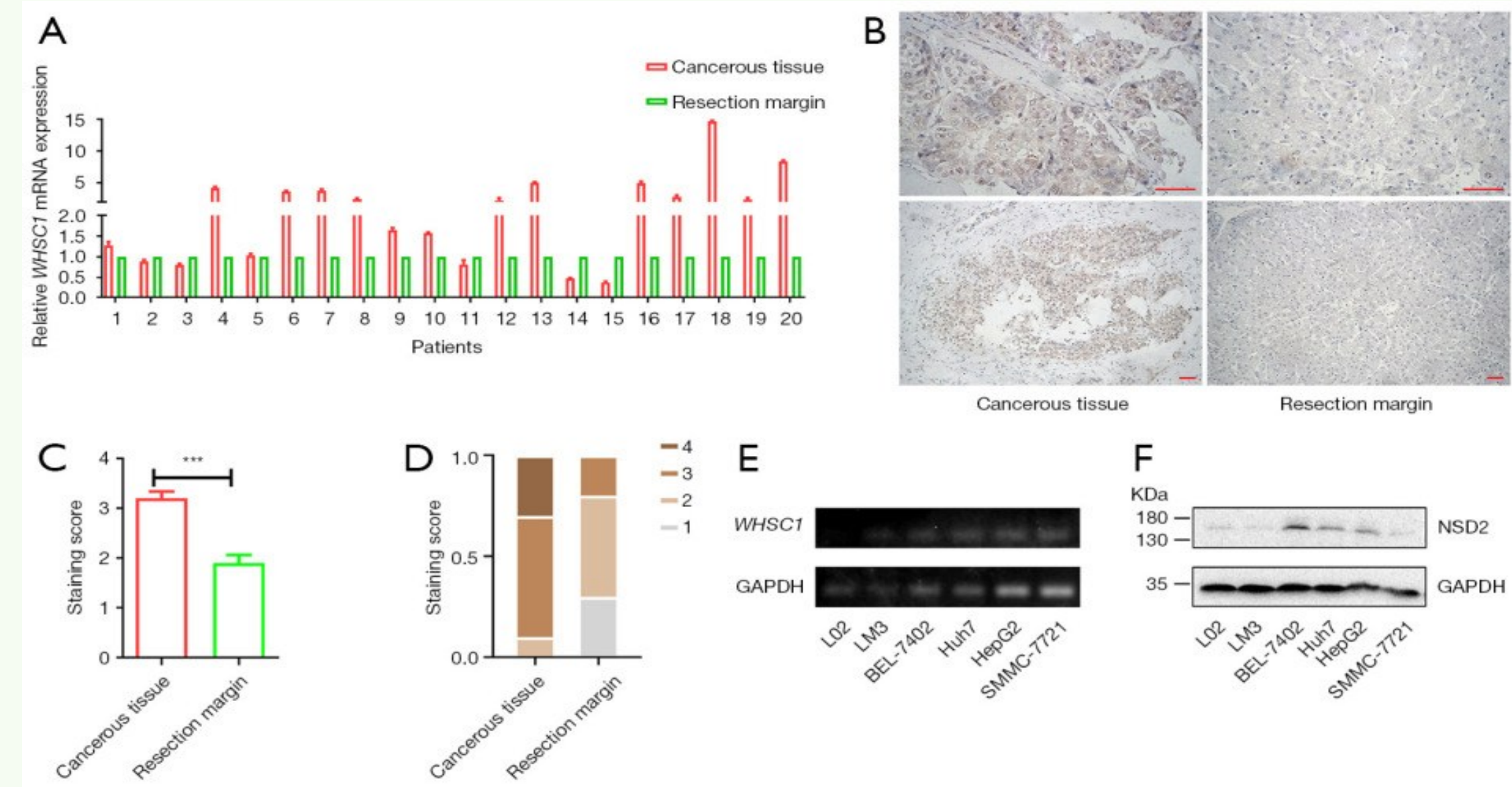
Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality globally, with limited therapeutic options available for advanced stages. Elucidating the molecular drivers of hepatocarcinogenesis holds promise for the development of targeted therapeutic strategies. Nuclear receptor-binding SET domain-containing protein 2 (NSD2), a histone lysine methyltransferase, is now recognized as a critical modulator of tumor progression. The aim of this study was to investigate the role of NSD2 in HCC.

Results

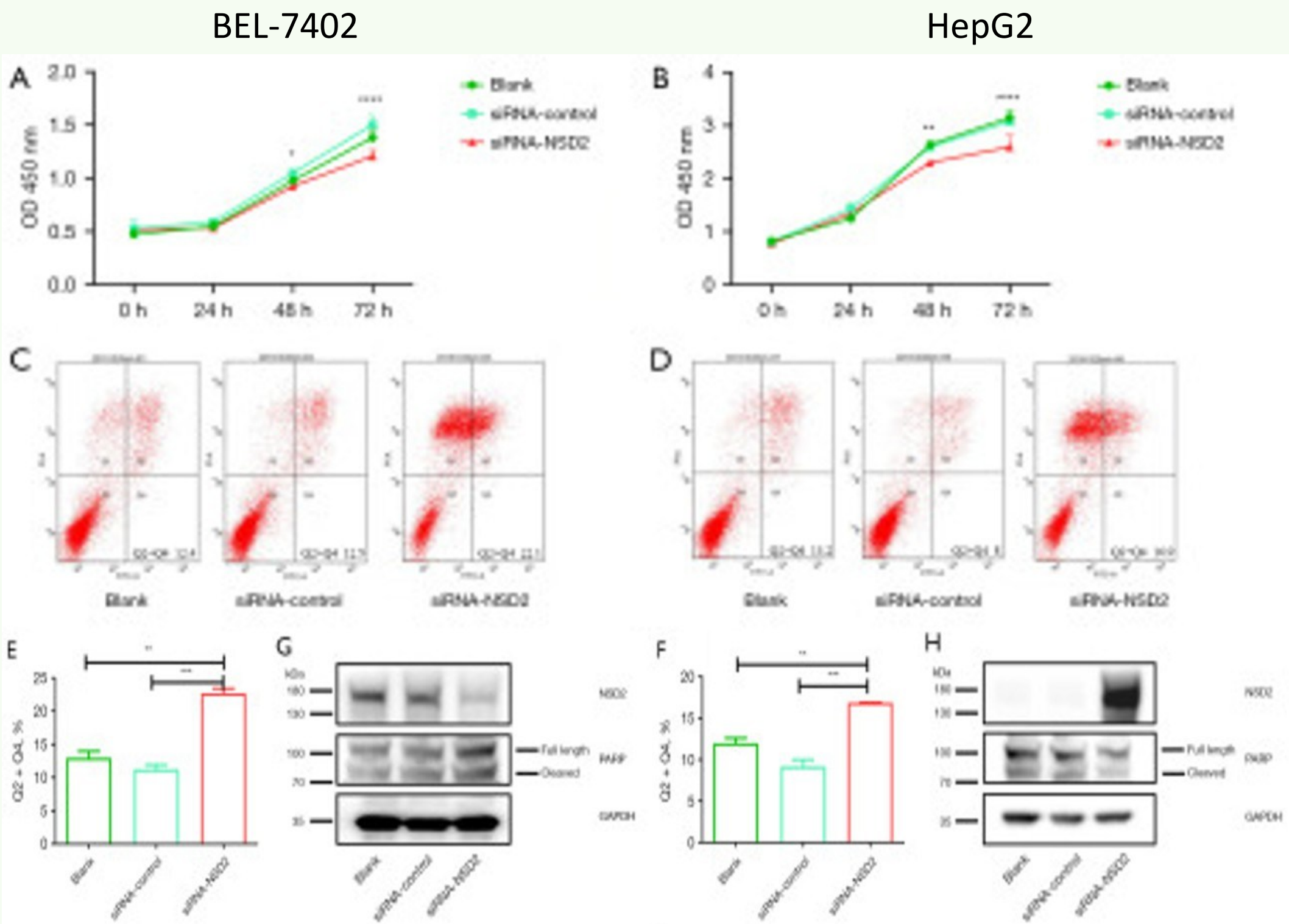
NSD2 expression is elevated in HCC and other cancers



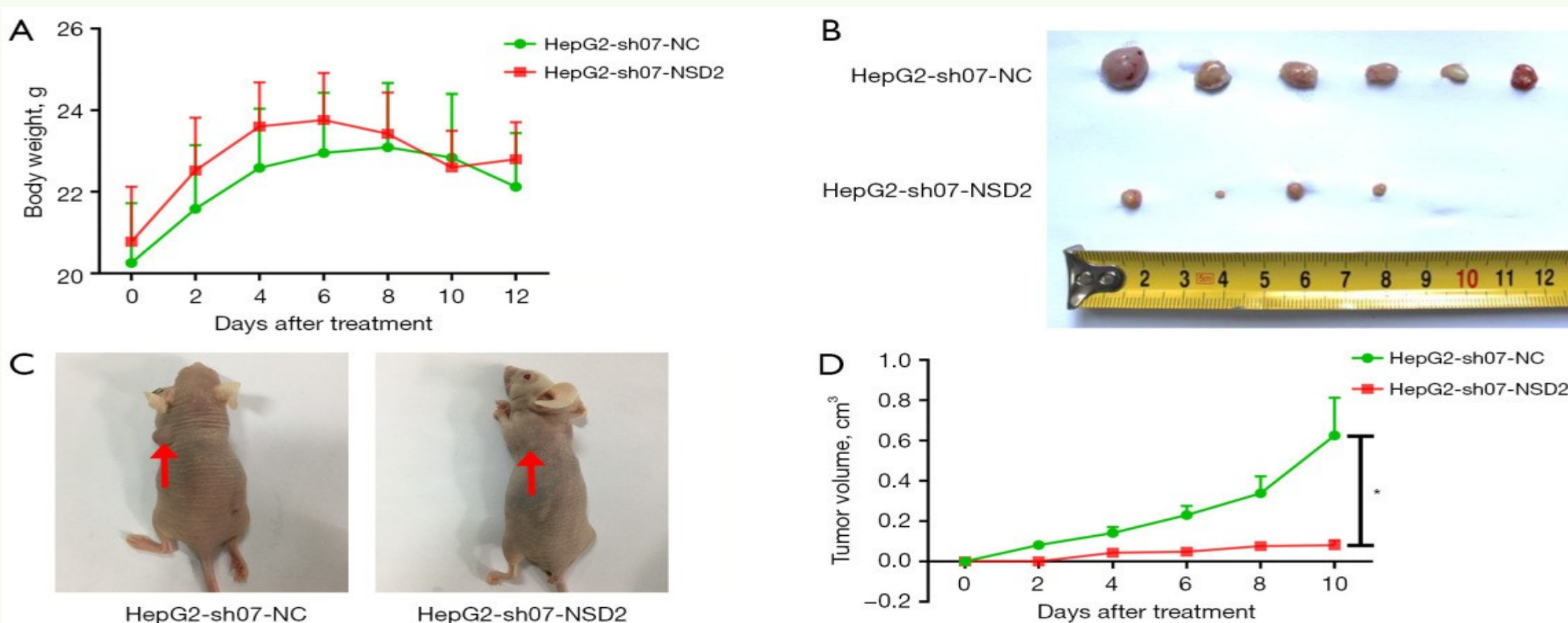
NSD2 expression is increased in HCC patients and cell lines



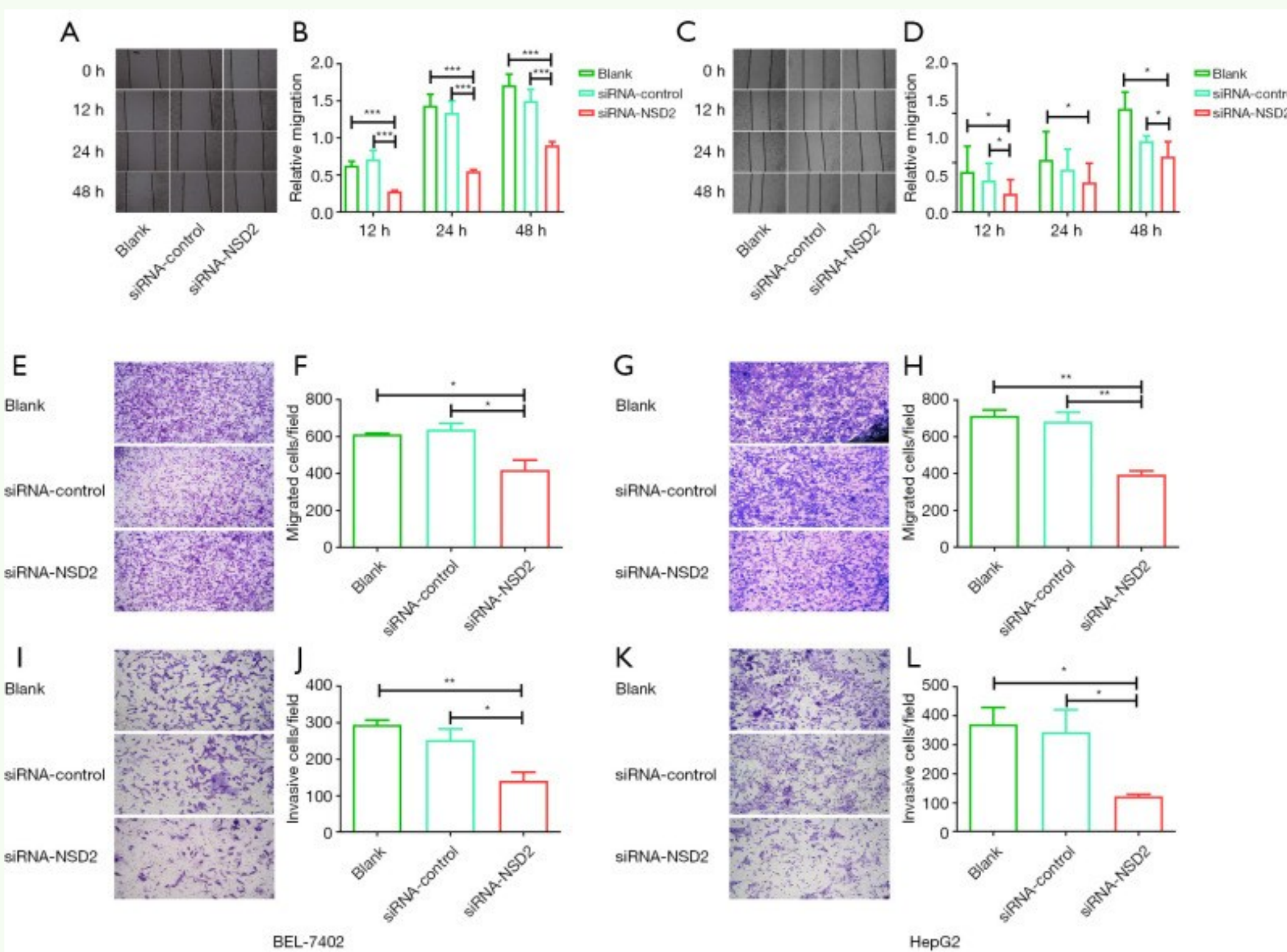
NSD2 promotes the proliferation and inhibites apoptosis of HCC cells in vitro



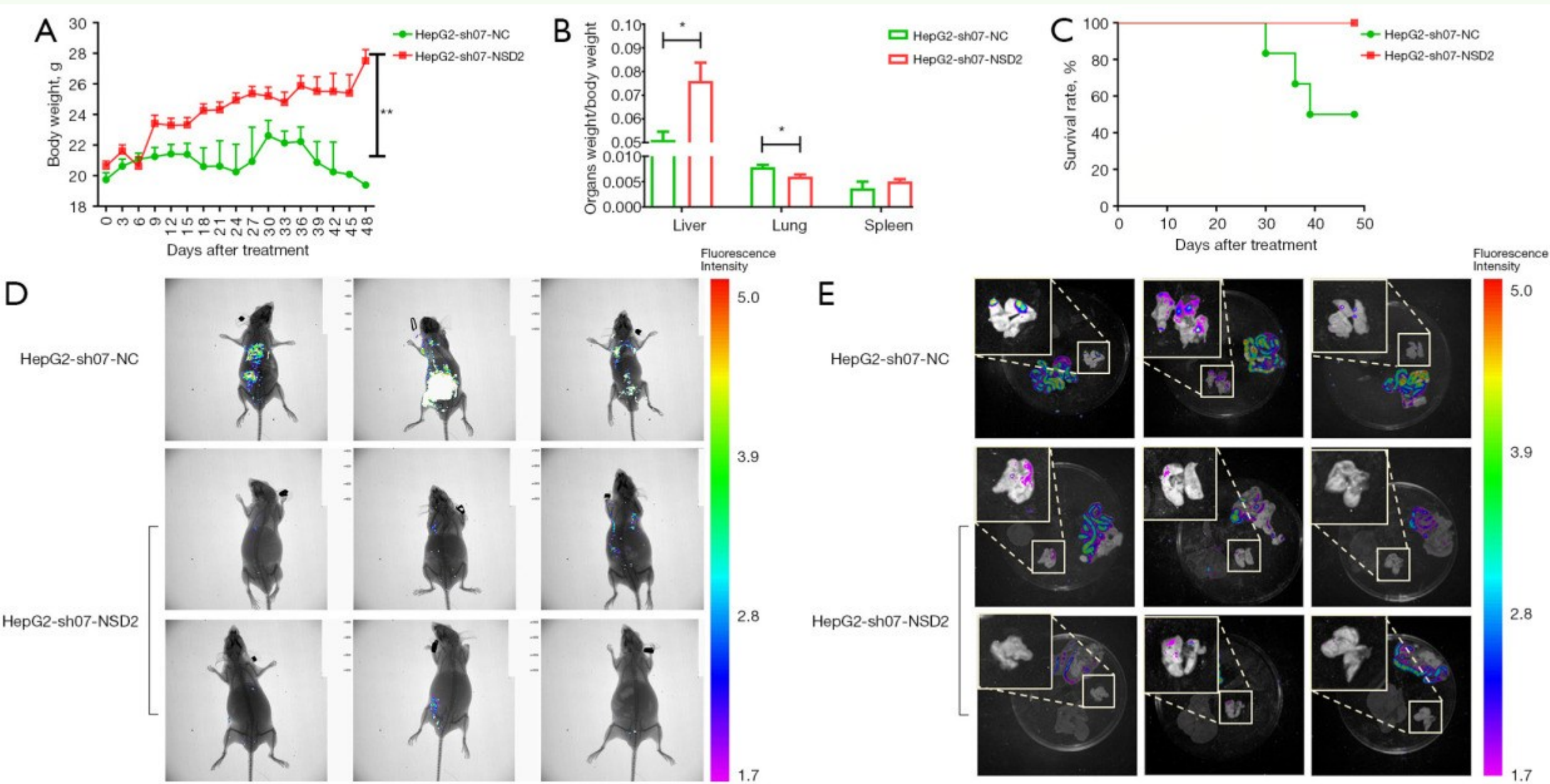
NSD2 promotes HCC tumorigenesis in vivo



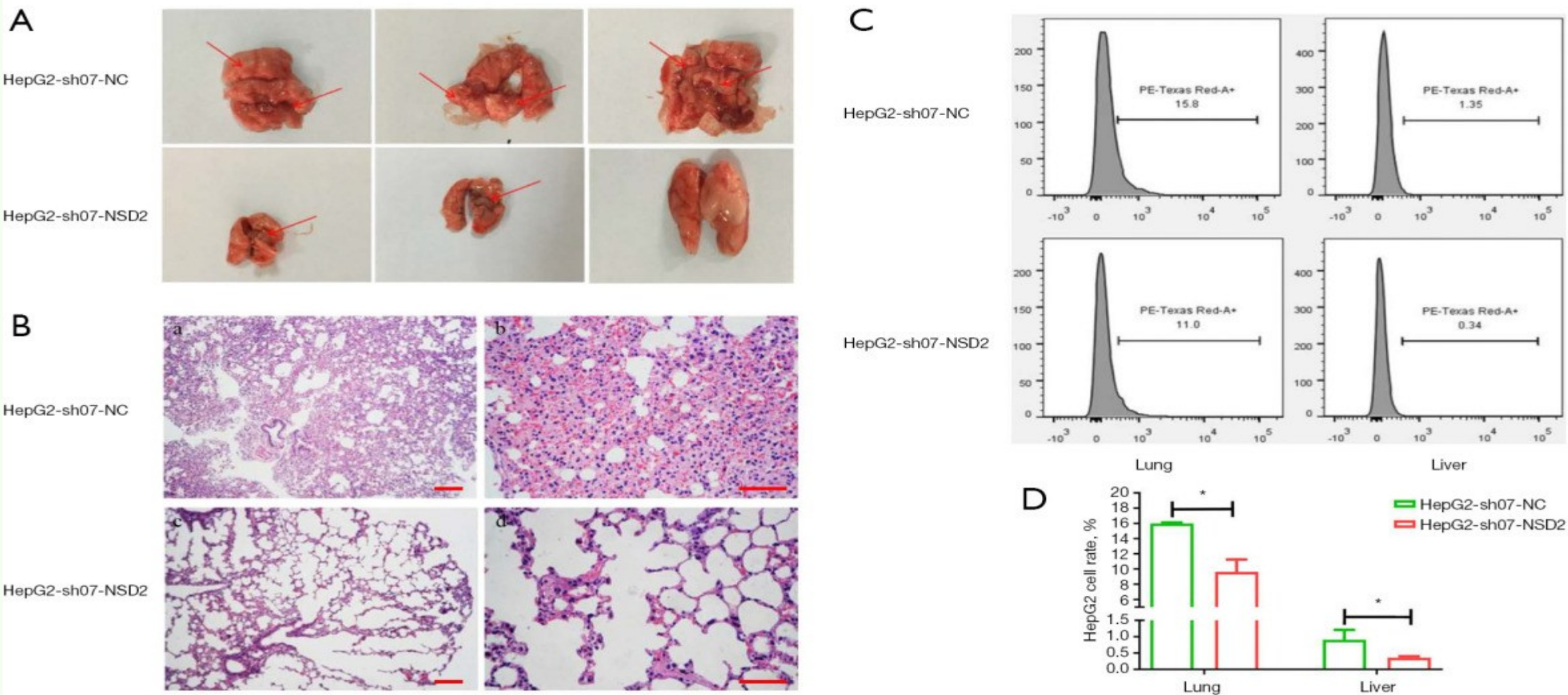
NSD2 promotes migration and invasion in HCC cells



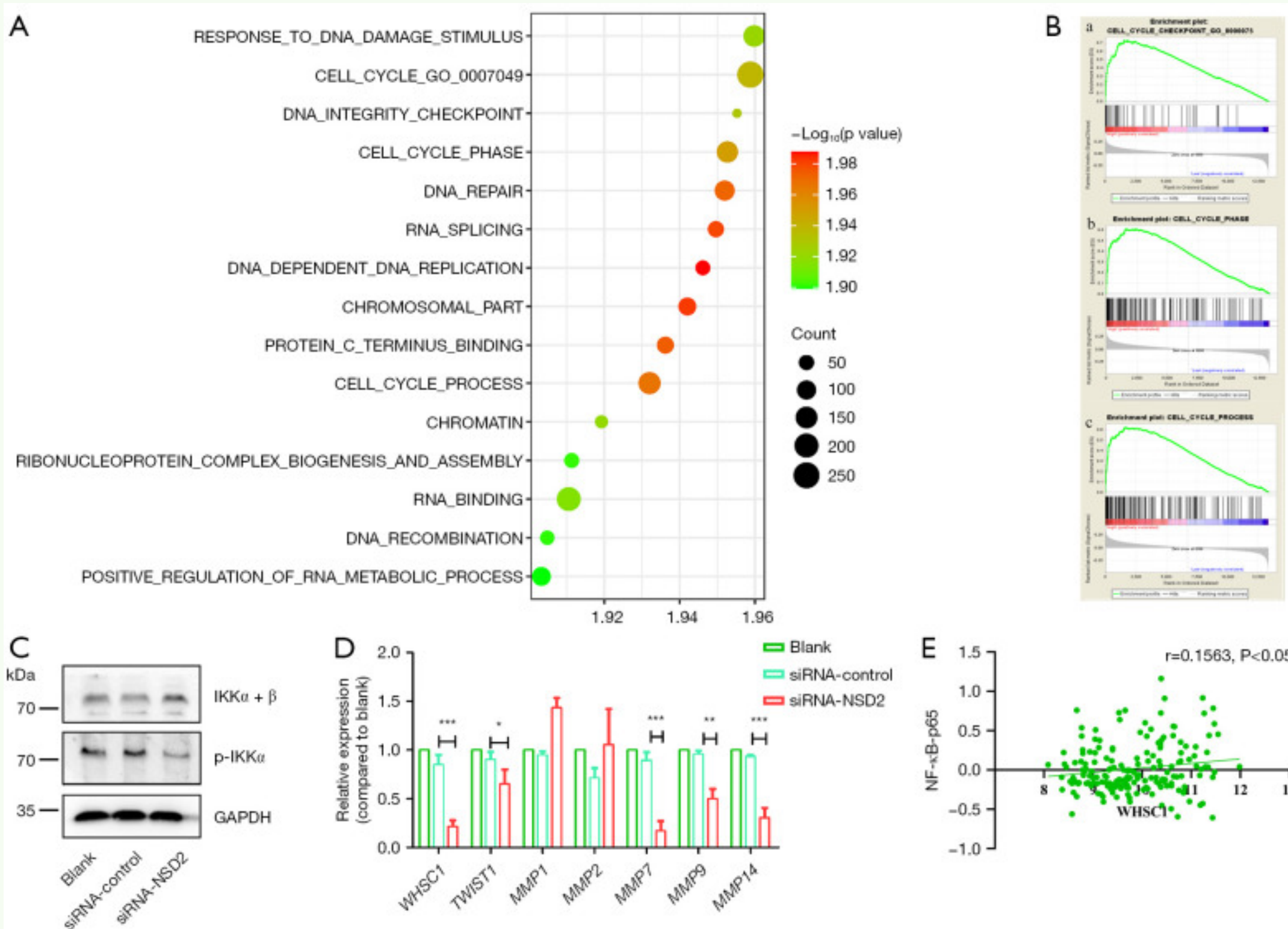
NSD2 regulates HCC cell metastasis and invasion in vivo



NSD2 regulates the invasion of HCC cells into the lung



NSD2 regulates HCC cell proliferation, migration and invasion via NF-κB and MMPs activation



Conclusions

- ✓ Depletion of NSD2 restrains HCC cells from in vitro and in vivo oncogenic phenotypes
- ✓ NSD2 mediates tumorigenesis through NF-κB and MMPs activation
- ✓ NSD2 can act as a master regulator driving HCC pathogenesis, suggesting its potential as a prognostic biomarker in cancer intervention