

A Dual-Targeting Ruthenium Nanodrug that Inhibits Primary Tumor Growth and Lung Metastasis by the PARP/ATM Pathway

Yu Lu

Capital Medical University

Di Zhu

Capital Medical University

Lin Gui

Capital Medical University

Yuanming Li

Peking Hospital

Wenjing Wang

Capital Medical University Youan Hospital

Jiawang Liu

University of Tennessee Health Science Center

Yuji Wang (✉ wangyuji@ccmu.edu.cn)

Capital Medical University <https://orcid.org/0000-0003-3842-7627>

Research

Keywords: Nanodrug, dual-targeting, lung, metastasis

Posted Date: June 26th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-36952/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Table 1. Stern-Volmer quenching constant (K_{sv} , $L \cdot mol^{-1}$), biomolecular quenching rate constant (K_q , $L \cdot mol^{-1} \cdot s^{-1}$), binding constant (K_b , $L \cdot mol^{-1}$) and the number of binding sites (n) of Ru complexes and human transferrin.

	$K_{sv} \cdot 10^5$	$K_q \cdot 10^{13}$	n	$K_b \cdot 10^5$
2b	1.09	1.89	1.1	3.97

Figures

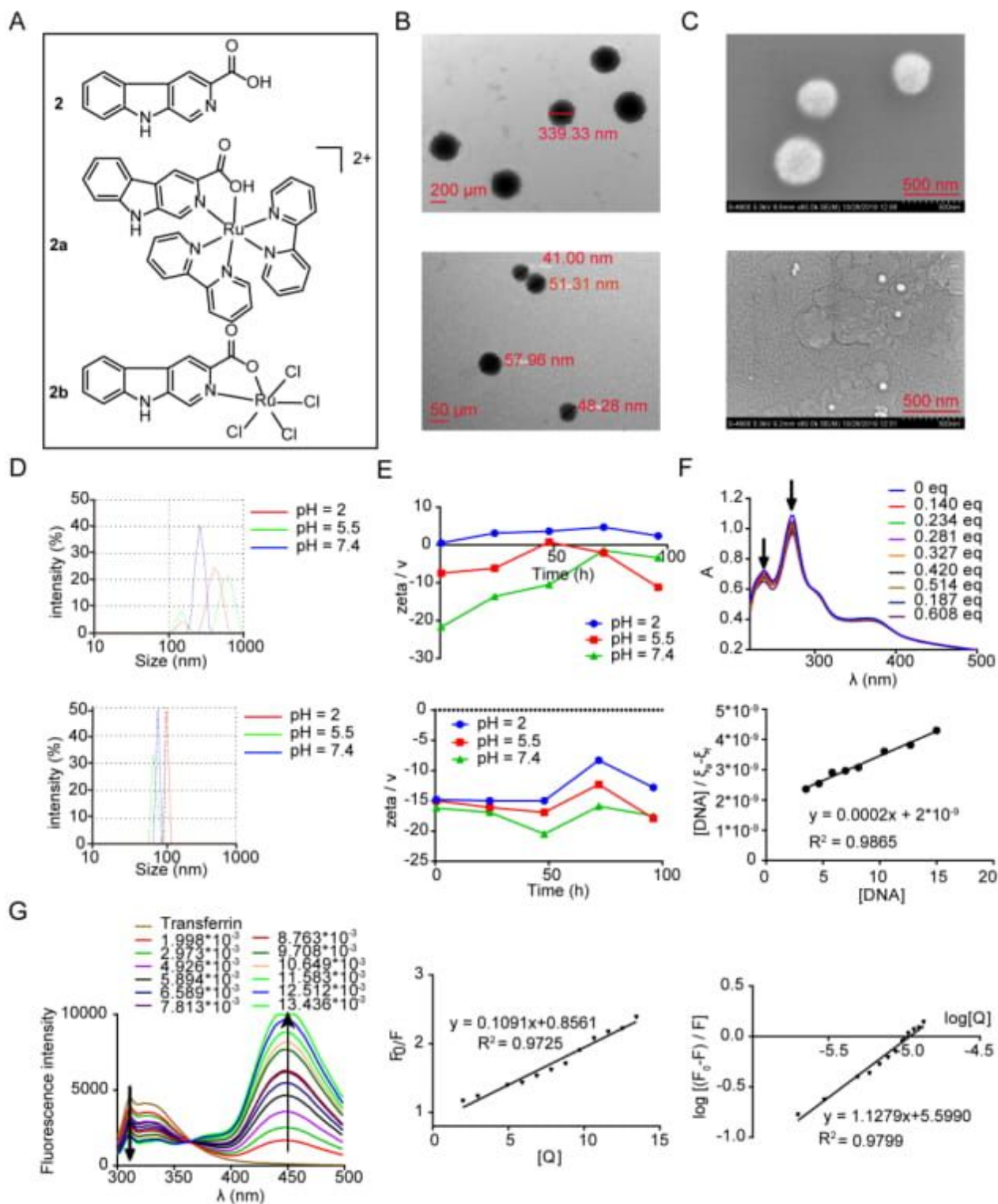


Figure 1

Physicochemical characterization of 2b. (A) Structure of 2, 2a and 2b. (B) TEM image of the Ru ligand 2 (up) and complex 2b (down). (C) SEM image of the Ru ligand 2 (up) and complex 2b (down). (D) Size of 2 (up) and 2b (down) at different pH values. (E) Zeta potentials of 2 (up) and 2b (down) at different pH

values within 96 h (detected at 0.5 h, 24 h, 48 h, 72 h and 96 h). (F) UV spectra of 2b with different concentrations of ctDNA. (G) Fluorescence emission spectra of hTF (0.4 μ M, λ_{ex} = 280 nm) with different concentrations of 2b. The classical Stern-Volmer equation and modified Stern-Volmer equation plots show tryptophan quenching in hTF.

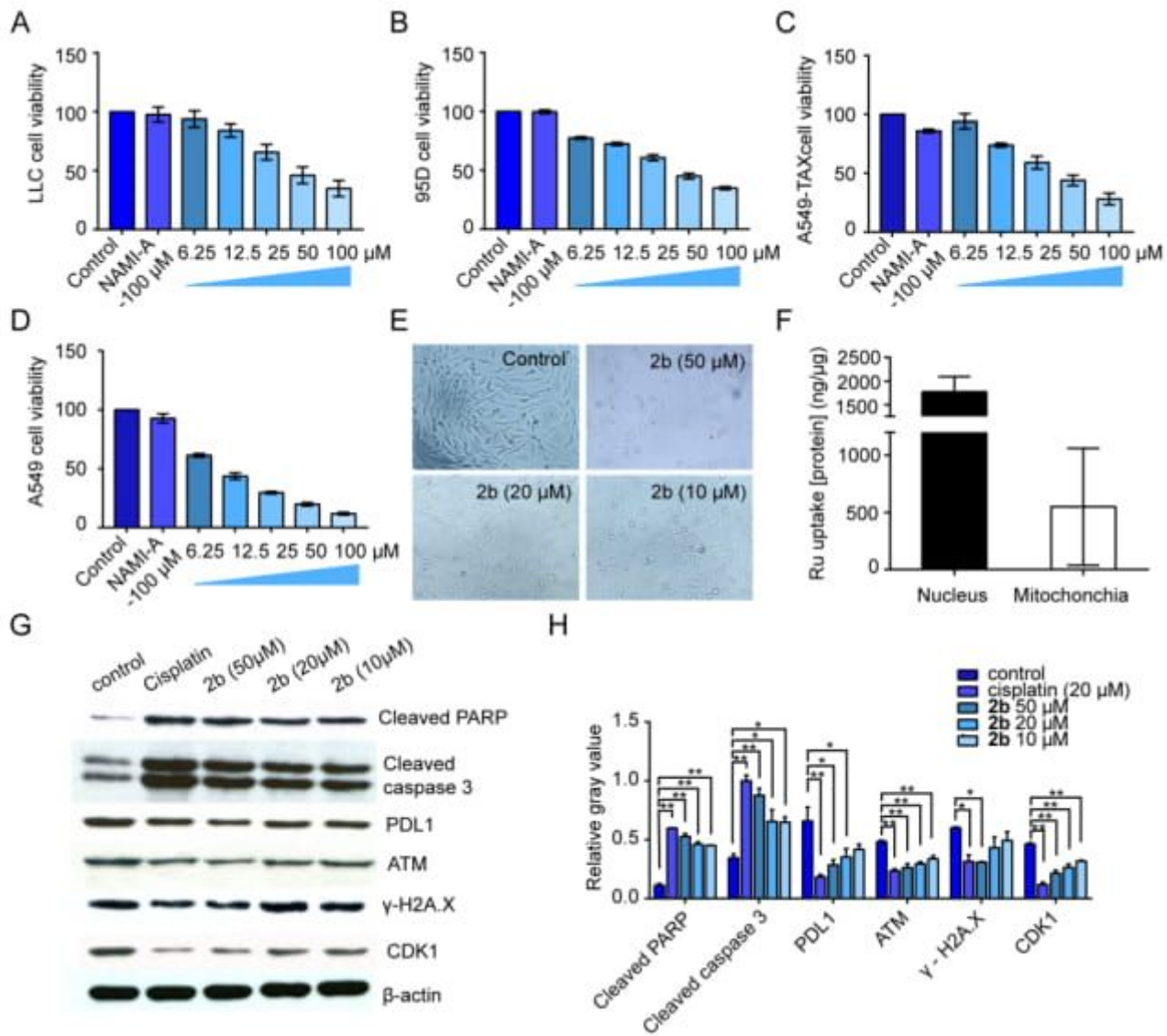


Figure 2

(A-D) Cell viability of LLC, 95D, A549-TAX and A549 cancer cells treated with different concentrations of 2b and 100 μ M NAMI-A. The concentrations of 2b were 6.25, 12.5, 25, 50, and 100 μ M. (E) Morphological changes in cells in the control and administration groups incubated with 5% CO₂ at 37 °C for 48 h. (F) The intracellular uptake of Ru in the 20 μ M group. (G-H) Western blotting image and relative gray value analysis of proteins in A549 cells treated with 2b.

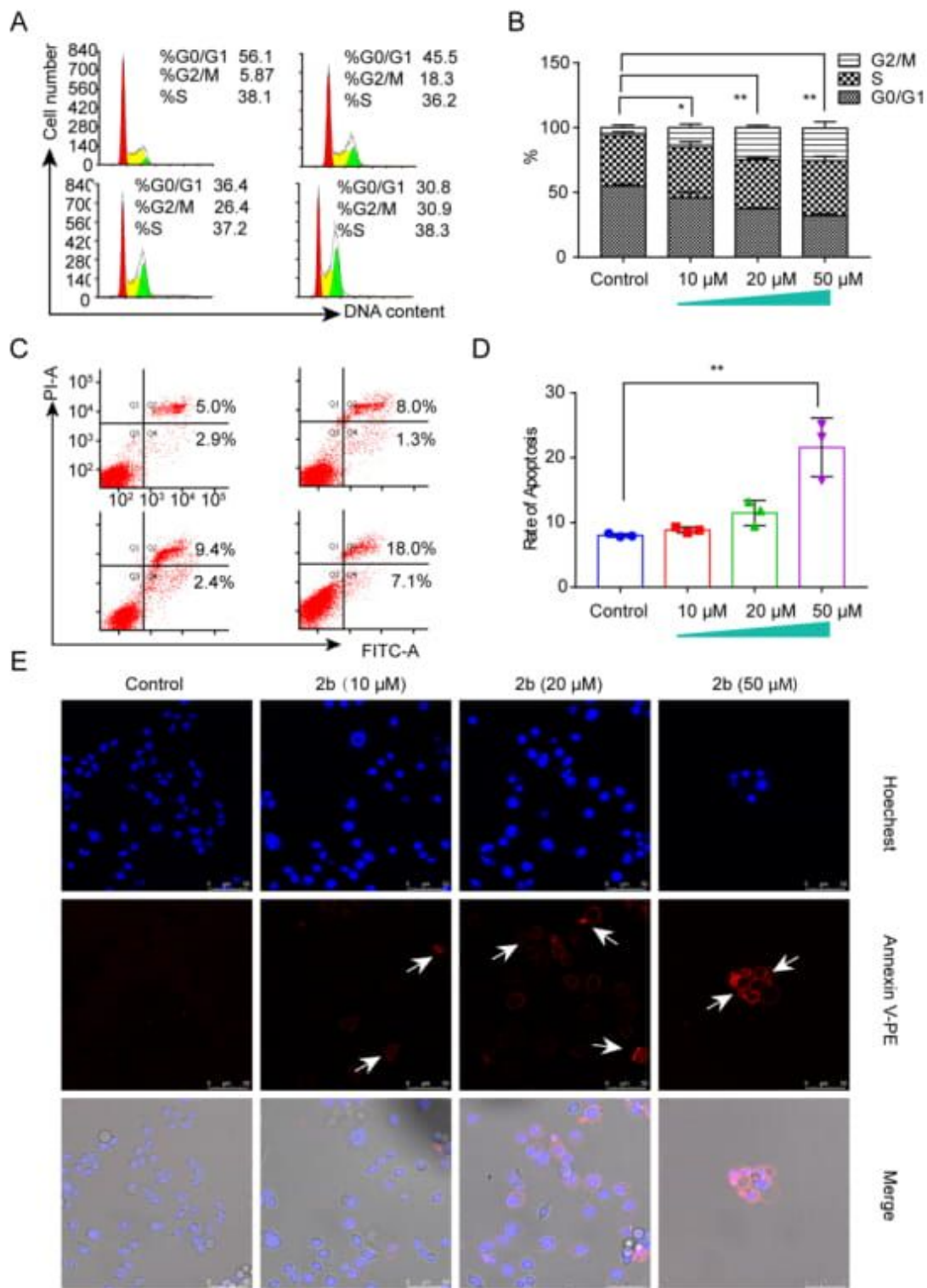


Figure 3

(A-B) Effect of 2b on the cell cycle. (C-D) Effect of 2b on cell apoptosis (Annexin V-FITC/PI, collected by flow cytometry). (E-F) Effect of 2b on cell apoptosis (Annexin V-PE/Hoechst, observed by confocal microscopy).

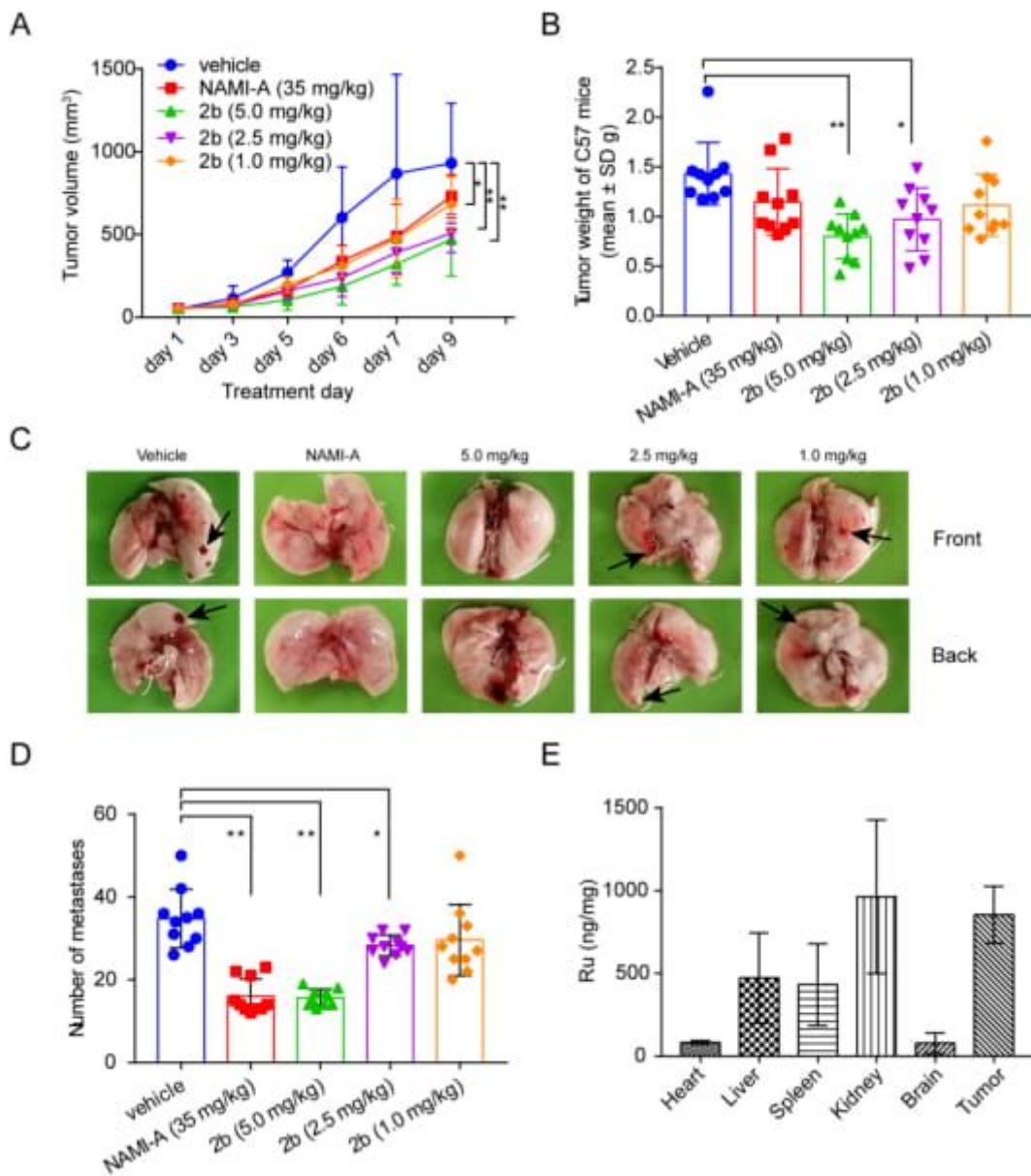


Figure 4

Effect of the Ru complex 2b on LLC tumor growth and metastasis in C57BL/6 mice. (A) Dose-dependent volume curve of LLC tumors. (B) Tumor weight of treated C57BL/6 mice. (C) Representative images of metastasis in the lung. (D) The number of metastases. (E) Body distribution of 2b (5.0 mg/kg). It is represented by the mean \pm SD (ng) of ruthenium per g of organ, n = 6.

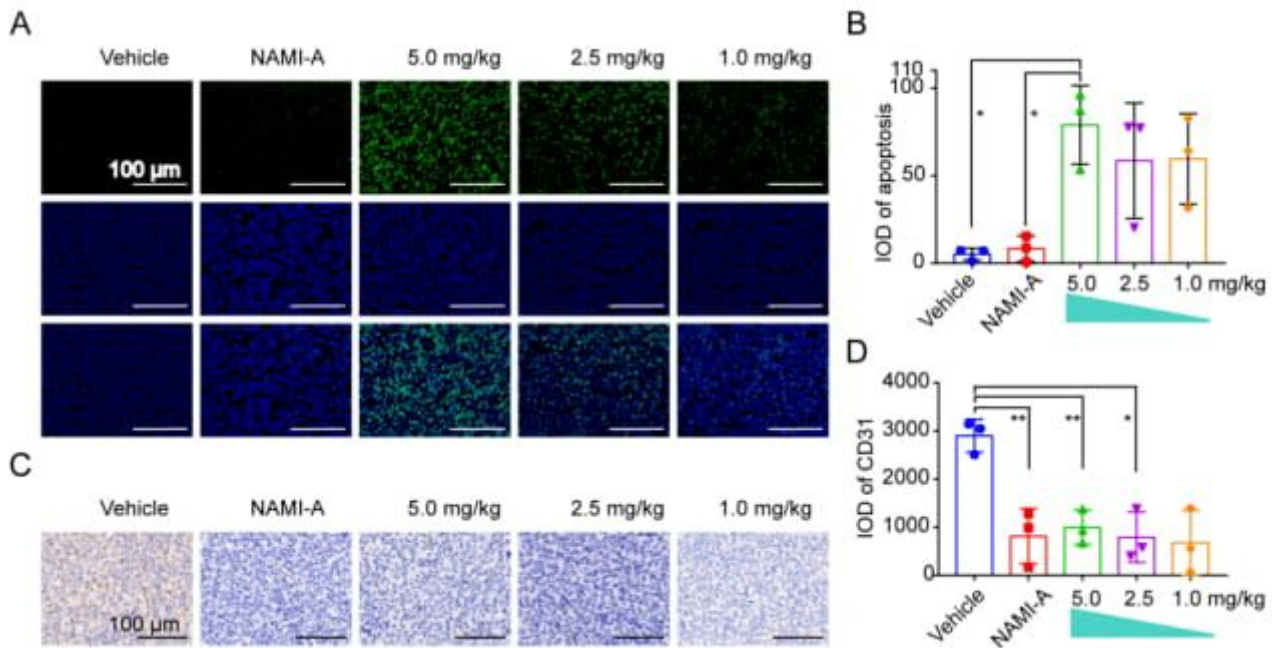


Figure 5

(A-B) Images and statistics of apoptosis tumor tissue apoptosis by TUNEL. (C-D) Image and statistics of CD31 expression in tumor tissue.

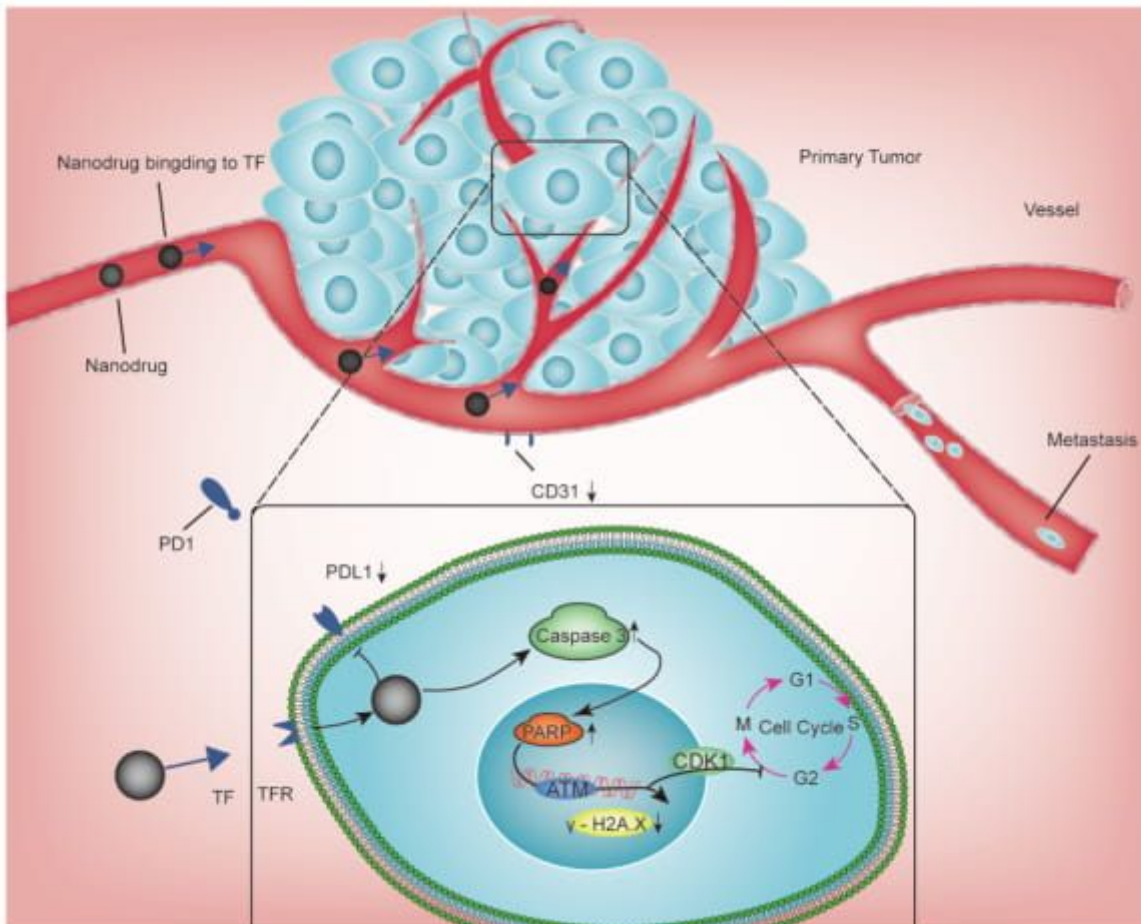


Figure 6

Mechanisms of complex 2b.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [3personalcover.pdf](#)
- [2supplementaryinformationluyu.pdf](#)