



EP02.05: SRPK1-Driven SND1 Subcellular Localization Promotes NSCLC Bone Metastasis via NPC-Mediated CIN-mRNA Export

上海市第一人民医院

SHANGHAI GENERAL HOSPITAL

上海交通大学医学院附属第一人民医院

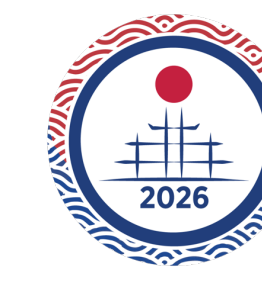
上海市红十字医院

Yi-zhe Ren¹, Lin Wang^{1,2}, Jia-tao Lou^{1,2*}

¹Department of Laboratory Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, 200080 Shanghai, China. ²College of Health Science and Technology, Shanghai Jiao Tong University

School of Medicine, Shanghai, 200080, China.

Correspondence: renyizhe1106@163.com



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INTRODUCTION

Patients with non-small cell lung cancer (NSCLC) often face high mortality and poor prognosis once the disease progresses to bone metastasis. Due to the current lack of stage-specific diagnostic biomarkers and effective therapeutic strategies, identifying the key molecular mechanisms driving bone metastasis and actionable targets is particularly urgent. Previous studies have indicated that nuclear envelope-associated proteins and their mediated nucleocytoplasmic transport play significant roles in lung cancer bone metastasis. Furthermore, protein post-translational modifications and subcellular localization to the nuclear envelope are crucial throughout NSCLC progression, including the bone-metastatic stage.

METHODS

To further investigate the key nuclear envelope-associated proteins and their mechanisms driving lung cancer bone metastasis, this study isolated nuclear envelope fractions from the parental lung cancer cell line H460 and its bone-metastatic subline H460-BM for proteomic analysis. By integrating prognostic data and gene expression profiles from the TCGA database for NSCLC, we identified SND1 as a potential key driver of bone metastasis.

DISCUSSION AND CONCLUSION

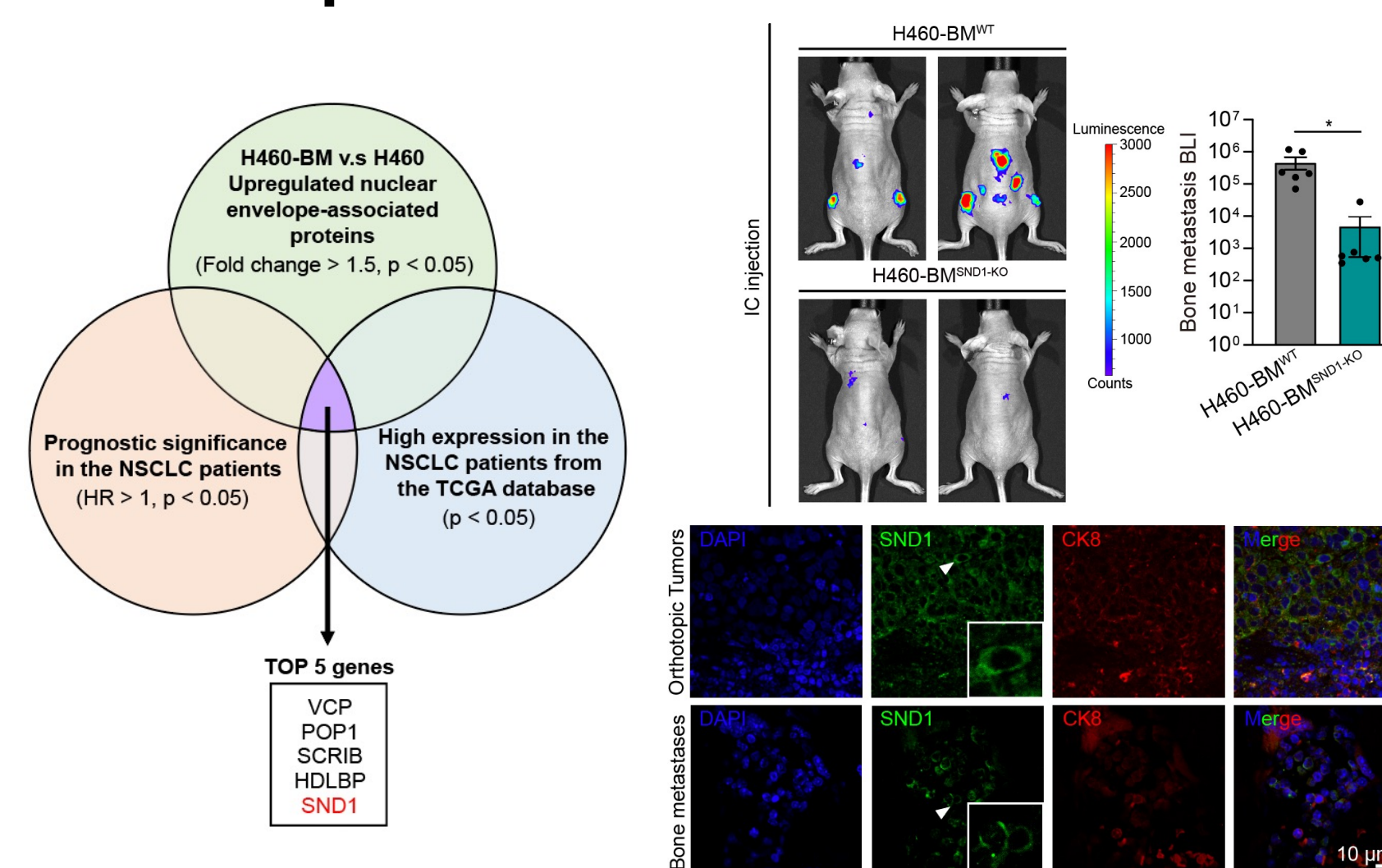
Post-translational modification promotes cancer by reprogramming protein subcellular localization:

- A novel SRPK1-SND1-cGAS-STING signaling axis that drives NSCLC bone metastasis.
- Providing potential biomarkers and therapeutic strategies for the prognosis and targeted treatment of NSCLC bone metastasis.

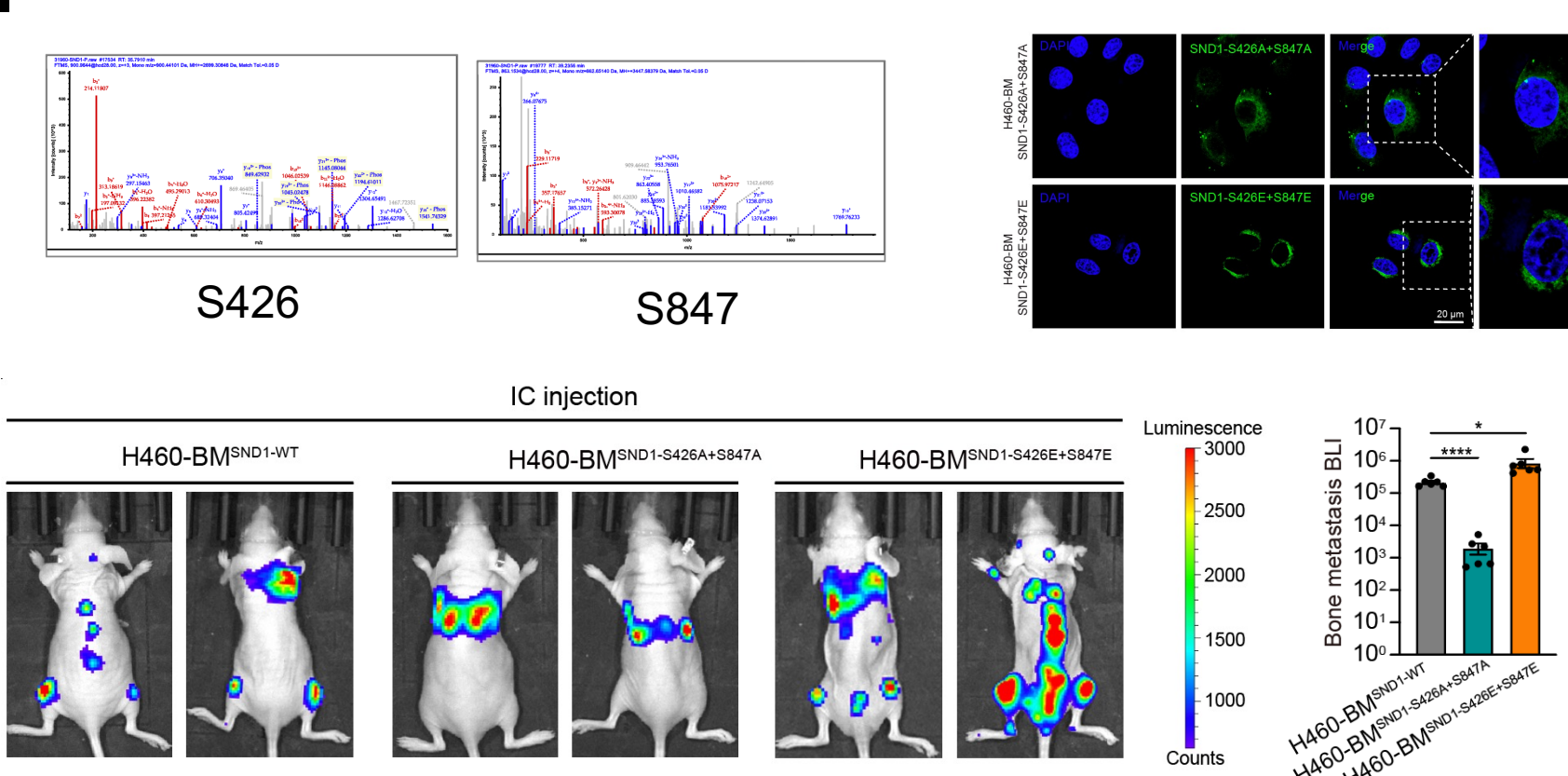
Key words: SND1, NSCLC bone metastasis, Nuclear envelope localization, cGAS-STING, Chromosomal instability

RESULTS

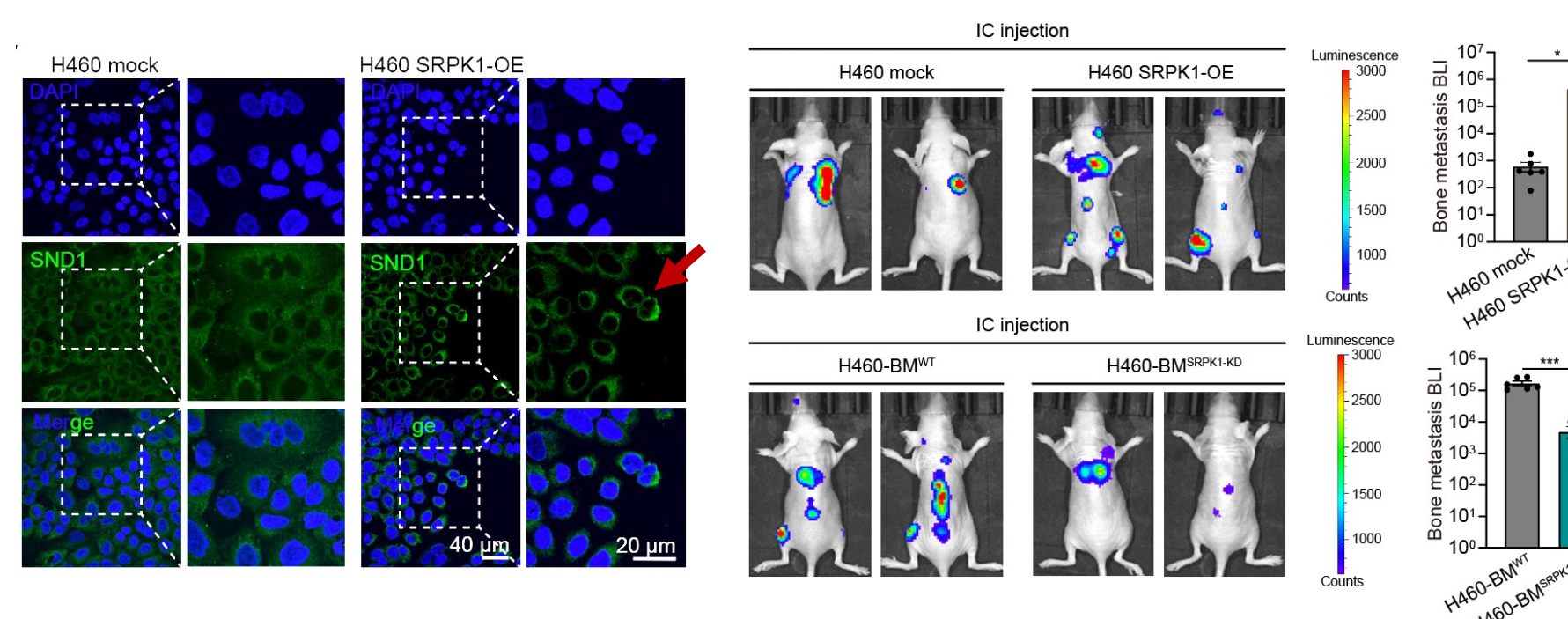
1. SND1 functions as a key nuclear envelope protein to promote bone metastasis in NSCLC.



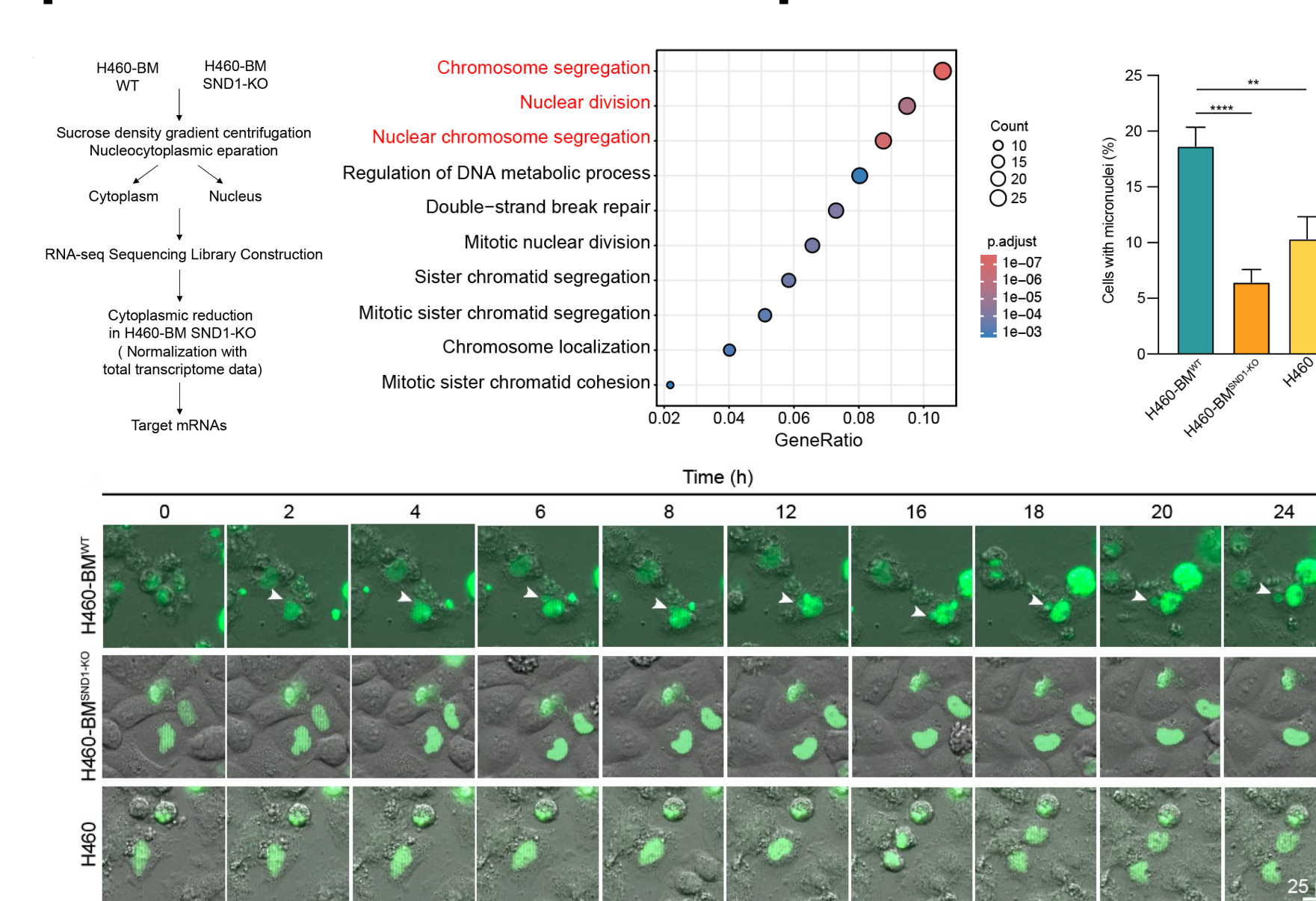
2. Phosphorylation of SND1 at serines 426 and 847 drives its nuclear envelope localization and promotes bone metastasis in NSCLC.



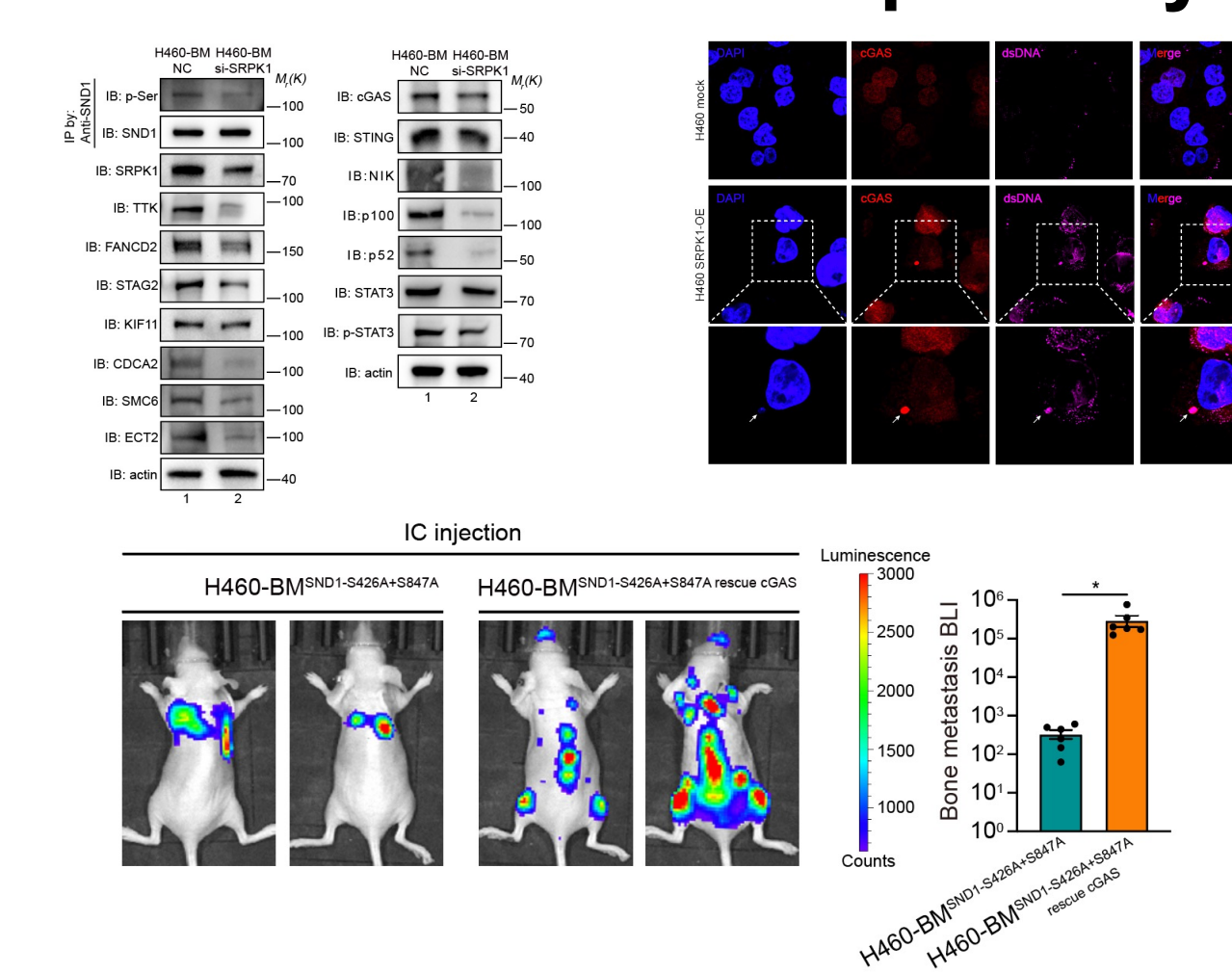
3. The phosphokinase SRPK1 mediates SND1 phosphorylation and promotes bone metastasis.



4. Nuclear membrane-localized SND1 promotes the nuclear export of CIN-mRNA.



5. The SRPK1-SND1-CIN signaling axis regulates the cGAS-STING pathway.



6. Targeted inhibition of the CIN-cGAS-STING signaling axis with small-molecule inhibitors alleviates lung cancer bone metastasis.

