

# P2.030: Targeting the TRIM–HIPK2 Axis Suppresses Slug-Driven Metastasis and Disrupts Mitochondrial Homeostasis in Lung Cancer

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## INTRODUCTION

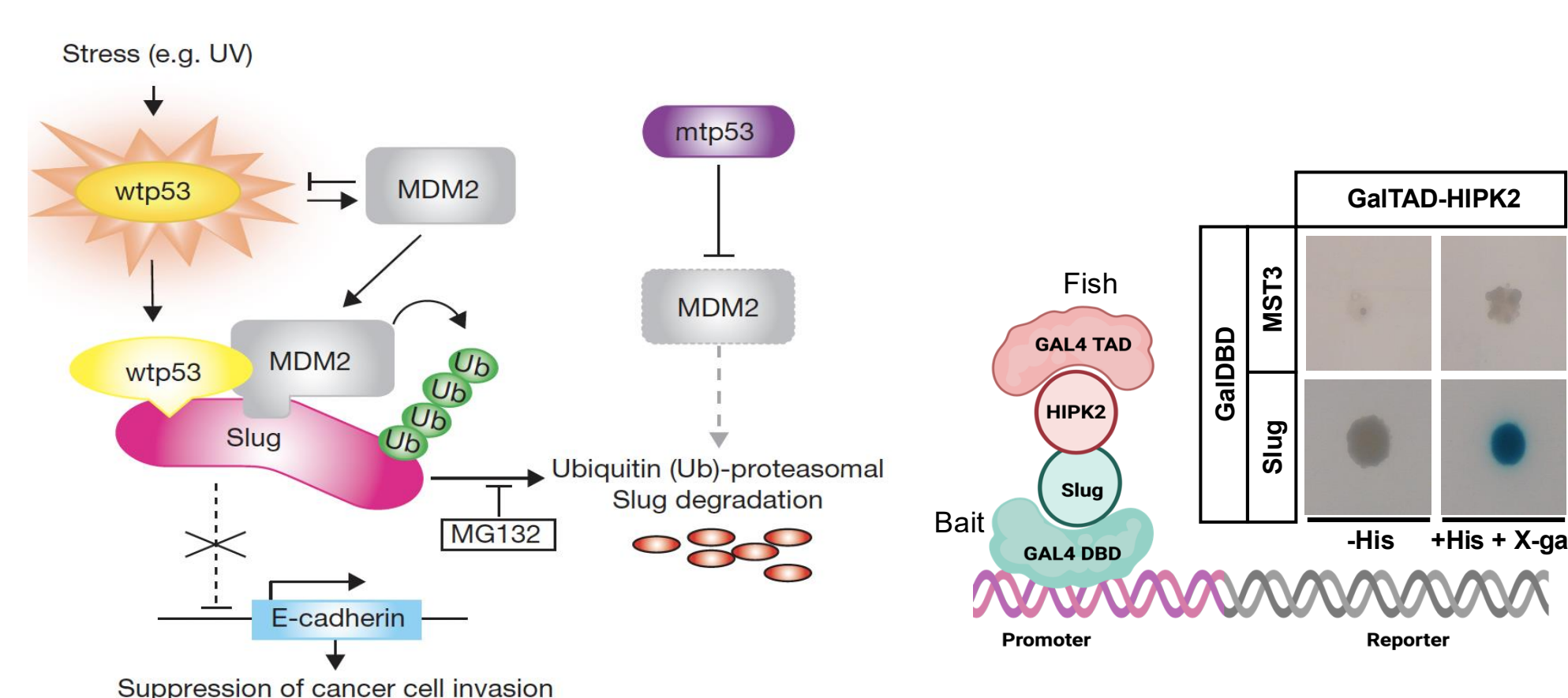
### Background

Lung cancer remains the leading cause of cancer-related death worldwide, and metastasis is a major driver of poor prognosis. EMT is a key process in metastatic progression, in which Slug (SNAIL2) acts as a master regulator promoting migration and invasion. Previously, we established that Slug abundance is controlled by ubiquitin-proteasome pathways, yet the upstream mechanisms that govern Slug degradation in physiological and pathological contexts remain incompletely understood.

### Hypothesis

In this study, we identify HIPK2 as a regulator of Slug stability and explore how HIPK2-dependent signaling intersects with mitochondrial stress programs that may influence Slug-driven metastatic phenotypes.

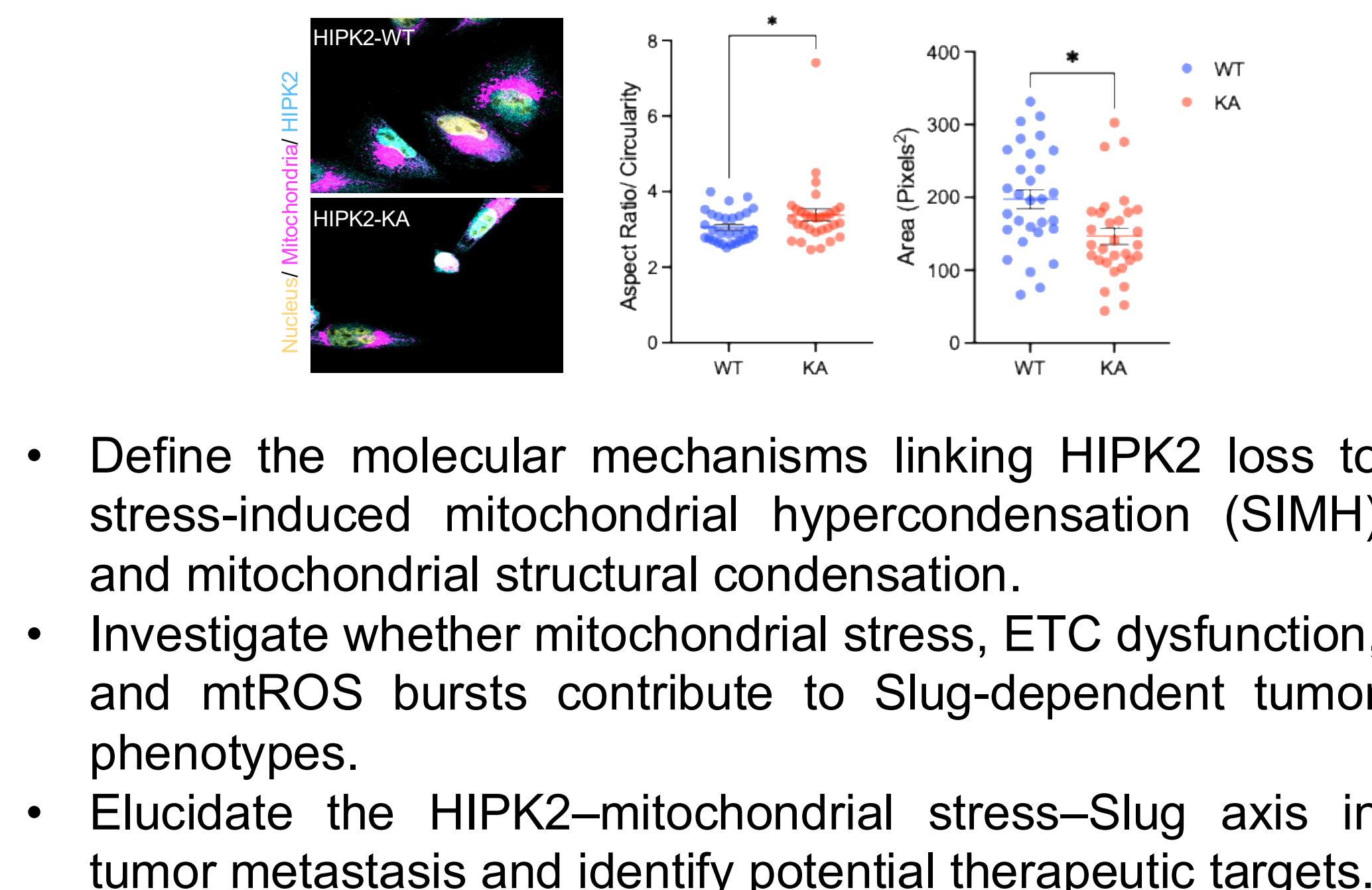
## STUDY DESIGN



Wang, S.P., Yang, P.-C. (2009) p53 controls cancer cell invasion by inducing the MDM2-mediated degradation of Slug. *Nature Cell Biology* 11: 694-704.

## FUTURE DIRECTIONS

### Preliminary data



- Define the molecular mechanisms linking HIPK2 loss to stress-induced mitochondrial hypercondensation (SIMH) and mitochondrial structural condensation.
- Investigate whether mitochondrial stress, ETC dysfunction, and mtROS bursts contribute to Slug-dependent tumor phenotypes.
- Elucidate the HIPK2–mitochondrial stress–Slug axis in tumor metastasis and identify potential therapeutic targets.

## RESULTS

Fig 1. HIPK2 and Slug Expression Are Associated with LUAD Prognosis.

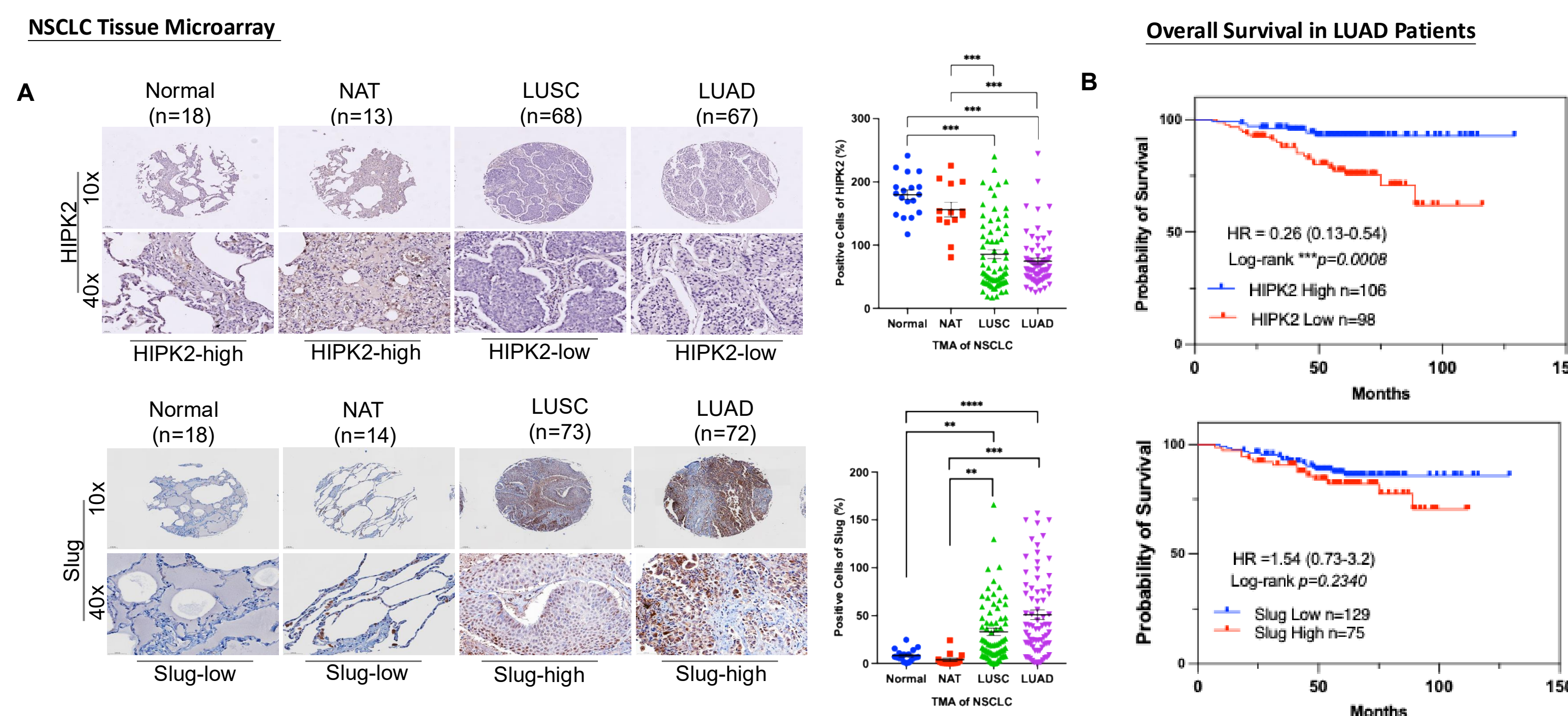


Fig 2. HIPK2 Phosphorylates and Stabilizes Slug.

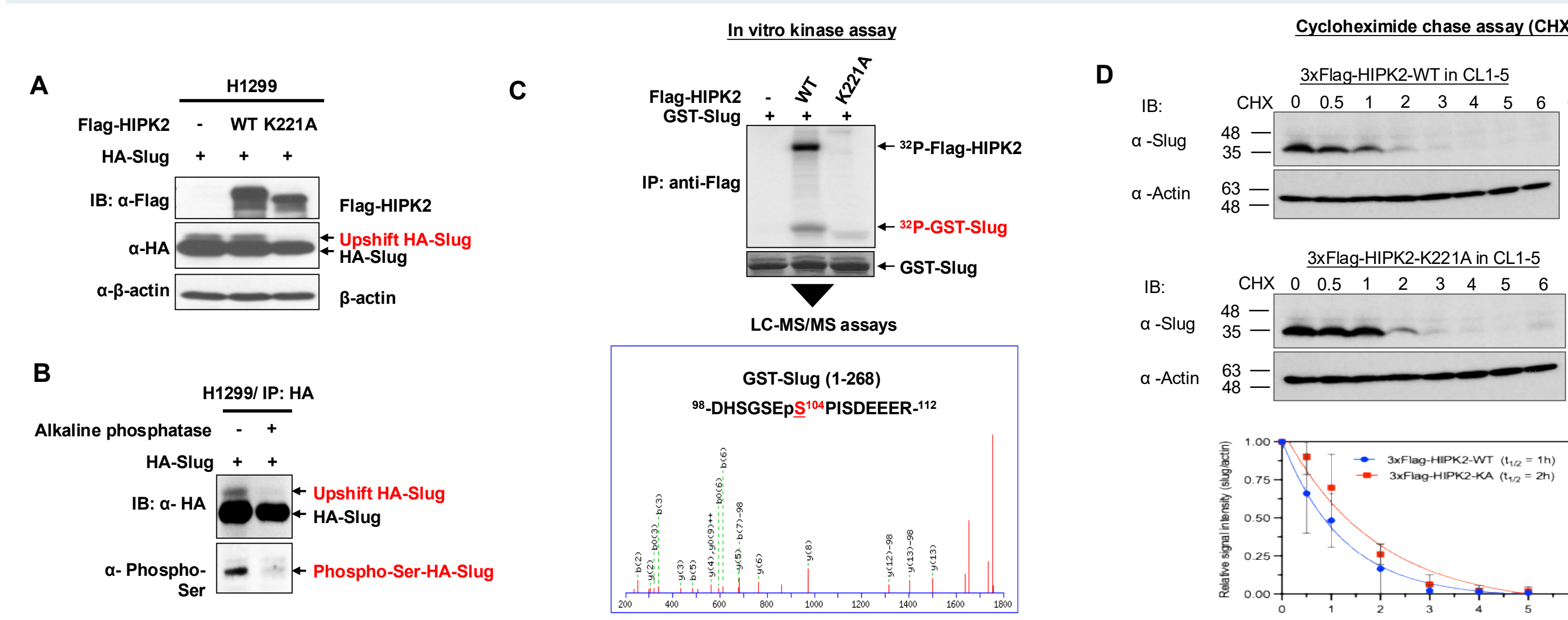


Fig 3. HIPK2 Kinase Activity Suppresses Lung Tumor Growth and Prolongs Survival In Vivo.

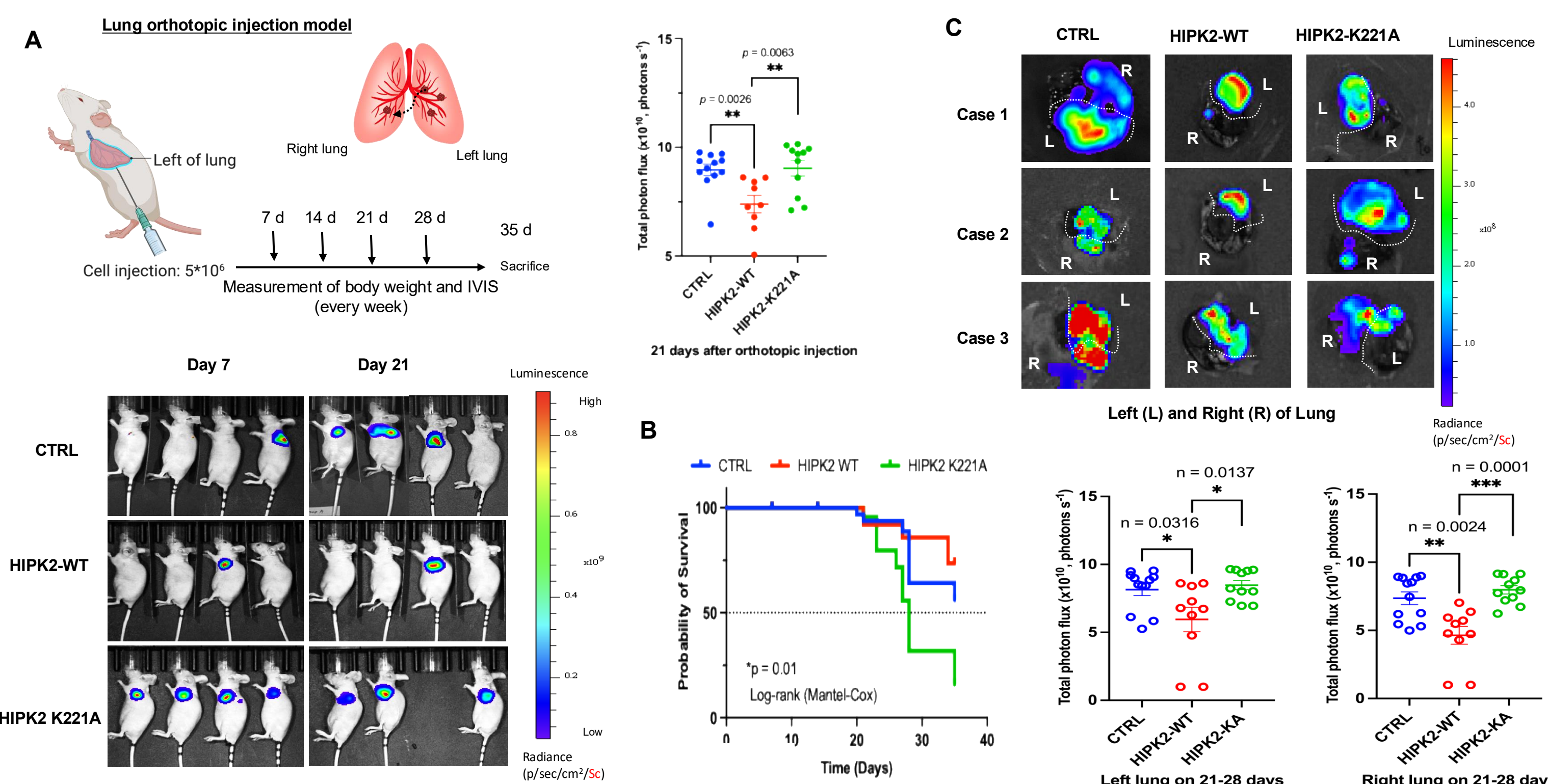
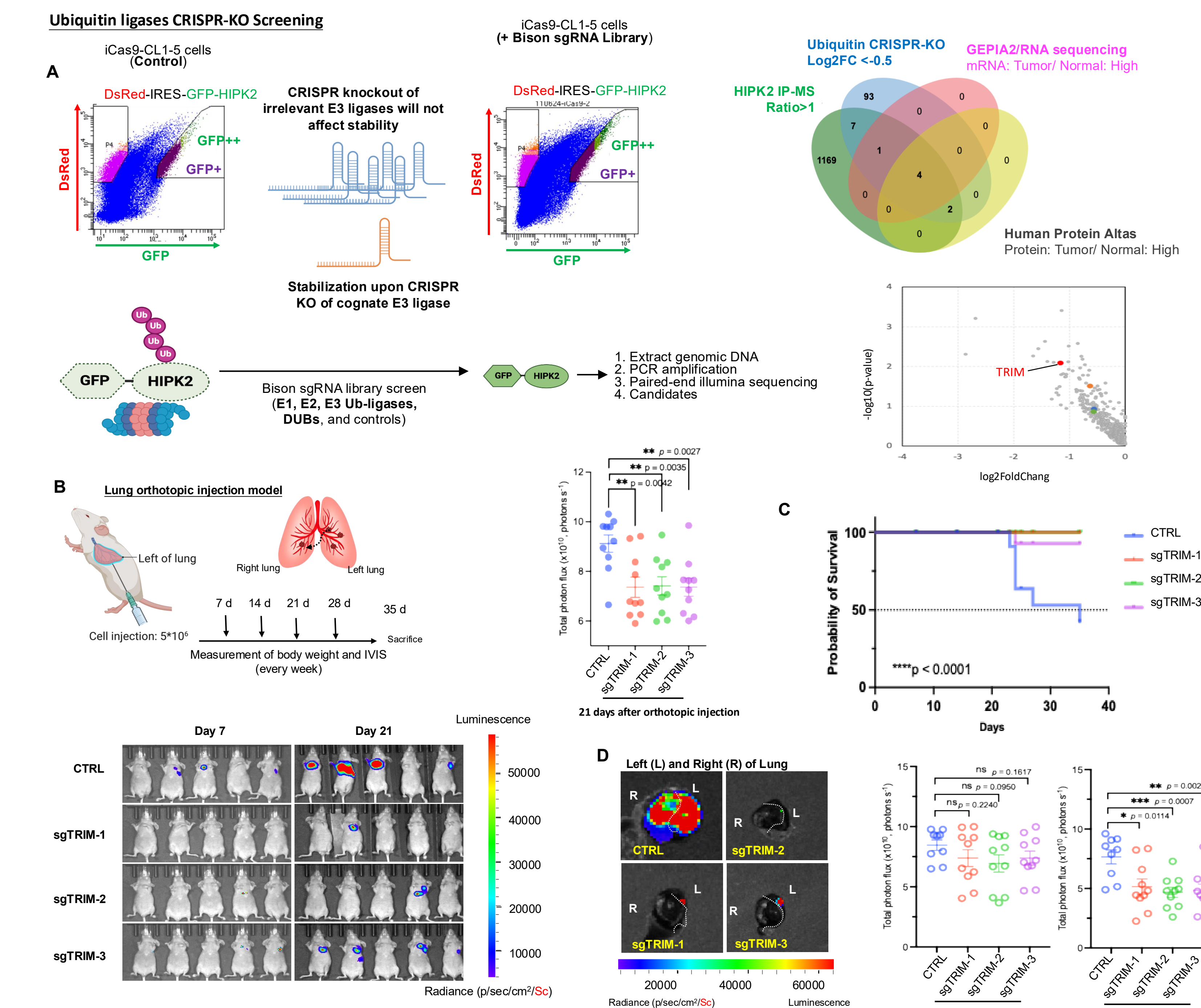
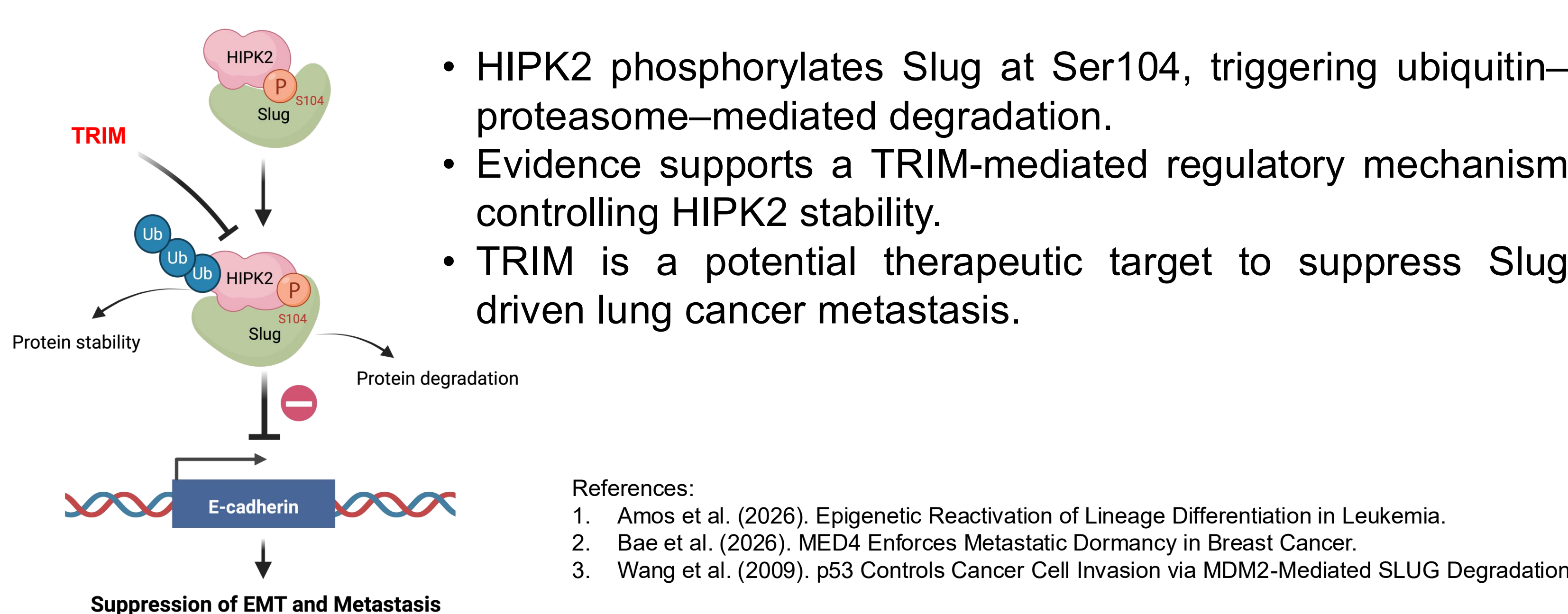


Fig 4. CRISPR Screening Reveals TRIM as a Regulator of HIPK2 Stability and Lung Tumor Growth.



## CONCLUSION



- References:
- Amos et al. (2026). Epigenetic Reactivation of Lineage Differentiation in Leukemia.
  - Bae et al. (2026). MED4 Enforces Metastatic Dormancy in Breast Cancer.
  - Wang et al. (2009). p53 Controls Cancer Cell Invasion via MDM2-Mediated SLUG Degradation.

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