



山东大学齐鲁第二医院
The Second Qilu Hospital of Shandong University

P2.033: CircDNAH14-encoded novel protein activates MTA1/EMT axis via antagonizing TRIM25 to promote NSCLC malignant progression

Presenting Peichao Li¹, Jie Zhou¹, Yuanhao Zhao¹, Qingkun Cui¹, Yilin Zhu¹, Yongjia Zhou¹, Lingxiao Yang¹, Yi Ding¹, Yongjie Wang², Yunpeng Zhao¹, Huiqing Yuan¹, Zhirong Qian³, Zhongxian Tian¹, Xiaogang Zhao¹
¹The Second Qilu Hospital of Shandong University, Jinan/CN, ²The Affiliated Hospital of Qingdao University, Qingdao/CN, ³The Seventh Affiliated Hospital of Sun Yat Sen University, Shenzhen/CN
Correspondence: lipeichao@email.sdu.edu.cn, zhaoxiaogang@sdu.edu.cn



IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Products encoded by circular RNAs (circRNAs) are reshaping our understanding of non-coding RNAs, with growing evidence linking them to tumor malignancy. In non-small cell lung cancer (NSCLC), however, the potential functions of circRNAs-encoded products remain largely unexplored. Herein, we found that circDNAH14, a cancer-promoting circRNA determined in our previous study, is functionally translated into a protein consisting of 373 amino acids (aa). We named this undefined circRNA-encoded protein as DNAH14-373aa, hereinafter abbreviated as D-373.

METHODS

Identification of circDNAH14-encoded D-373 protein

LC-MS/MS, polysome extraction coupled RT-qPCR, bicistronic reporter constructs and WB were employed to verify the D-373 protein.

Clinical significance

Spearman correlation analysis and Kaplan-Meier curves were applied to explore the clinical significance of D-373 based on its IHC score.

Functional assays

NSCLC cell lines, PDOs and mouse xenograft models were used to investigate the biological functions of D-373.

Molecular mechanism exploration

Co-IP, IF, RNA-seq, and protein-protein docking analyses were performed to dissect the underlying molecular mechanisms.

Drug-target binding validation

Virtual screening and BLI assays verified the direct drug-protein binding affinity.

RESULTS AND CONCLUSION

Results

CircDNAH14 encodes a previously uncharacterized protein, designated D-373. Clinical analysis confirmed that D-373 levels are closely associated with advanced NSCLC stages and predict unfavorable prognoses. The functional studies established D-373 as an oncogenic protein that drives NSCLC progression and cisplatin resistance. Mechanistically, D-373 competes with TRIM25 for interaction with MTA1, impairing ubiquitin-proteasome system (UPS)-mediated MTA1 degradation. Then, we determined that D-373 enhances NSCLC malignancy by modulating the MTA1-dependent epithelial-mesenchymal transition (EMT) progression. Furthermore, by performing FDA-approved drug screening, bio-layer interferometry (BLI) assays, and functional validation, we demonstrated that teniposide directly targets D-373 to block the D-373-mediated impairment of TRIM25-MTA1 interaction, thereby attenuating NSCLC progression by accelerating TRIM25-mediated MTA1 degradation.

Conclusion

These findings identify D-373 as an oncogenic circRNA-encoded protein and elucidate its regulation of the MTA1/EMT axis, suggesting a promising and druggable target for precise therapy of NSCLC.

REFERENCE & ACKNOWLEDGEMENTS

Reference

Liu, C.-X. and L.-L. Chen, Circular RNAs: Characterization, cellular roles, and applications. *Cell*, 2022. 185(12): p. 2016-2034.
Conn, V.M., A.M. Chinnaiyan, and S.J. Conn, Circular RNA in cancer. *Nature Reviews. Cancer*, 2024. 24(9): p. 597-613.
Xu, C., et al., MTA1 promotes metastasis of MPM via suppression of E-cadherin. *Journal of Experimental & Clinical Cancer Research : CR*, 2015. 34: p. 151.
Zhou, J., et al., Circ_16601 facilitates Hippo pathway signaling via the miR-5580-5p/FGB axis to promote my-CAF recruitment in the TME and LUAD progression. *Respiratory Research*, 2023. 24(1): p. 276.

Acknowledgement

We sincerely acknowledge all members from the Department of Thoracic Surgery in The Second Qilu Hospital of Shandong University.

FIGURES

Fig.1 CircDNAH14 was identified to encode a novel and oncogenic protein (D-373) in NSCLC

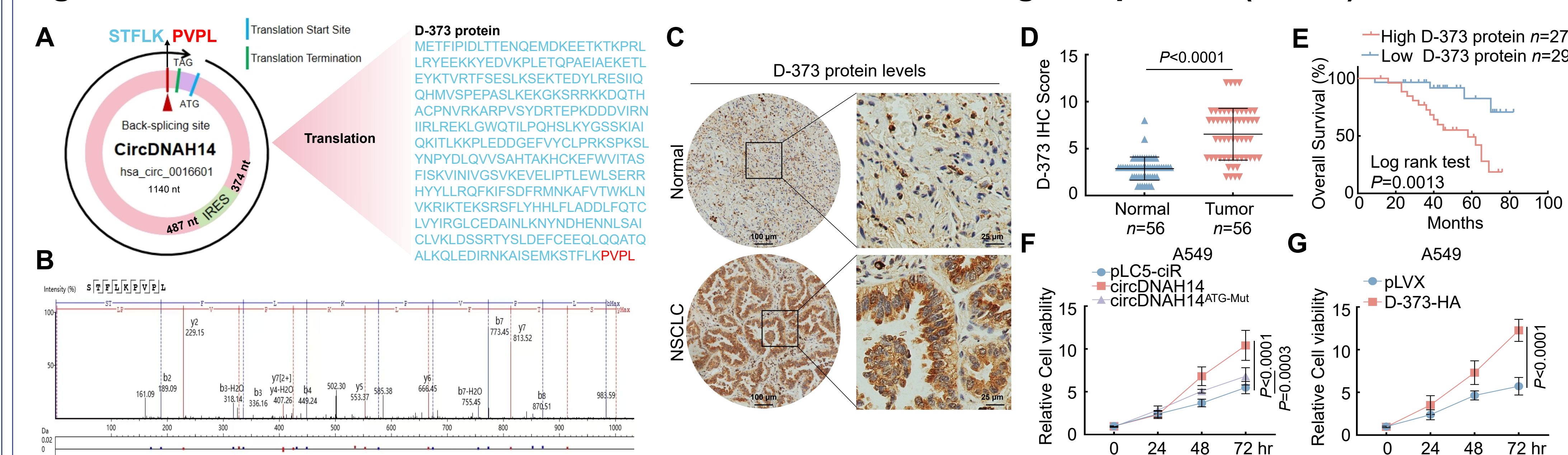


Fig.2 D-373 promotes progression of NSCLC by stabilizing MTA1 via antagonizing TRIM25

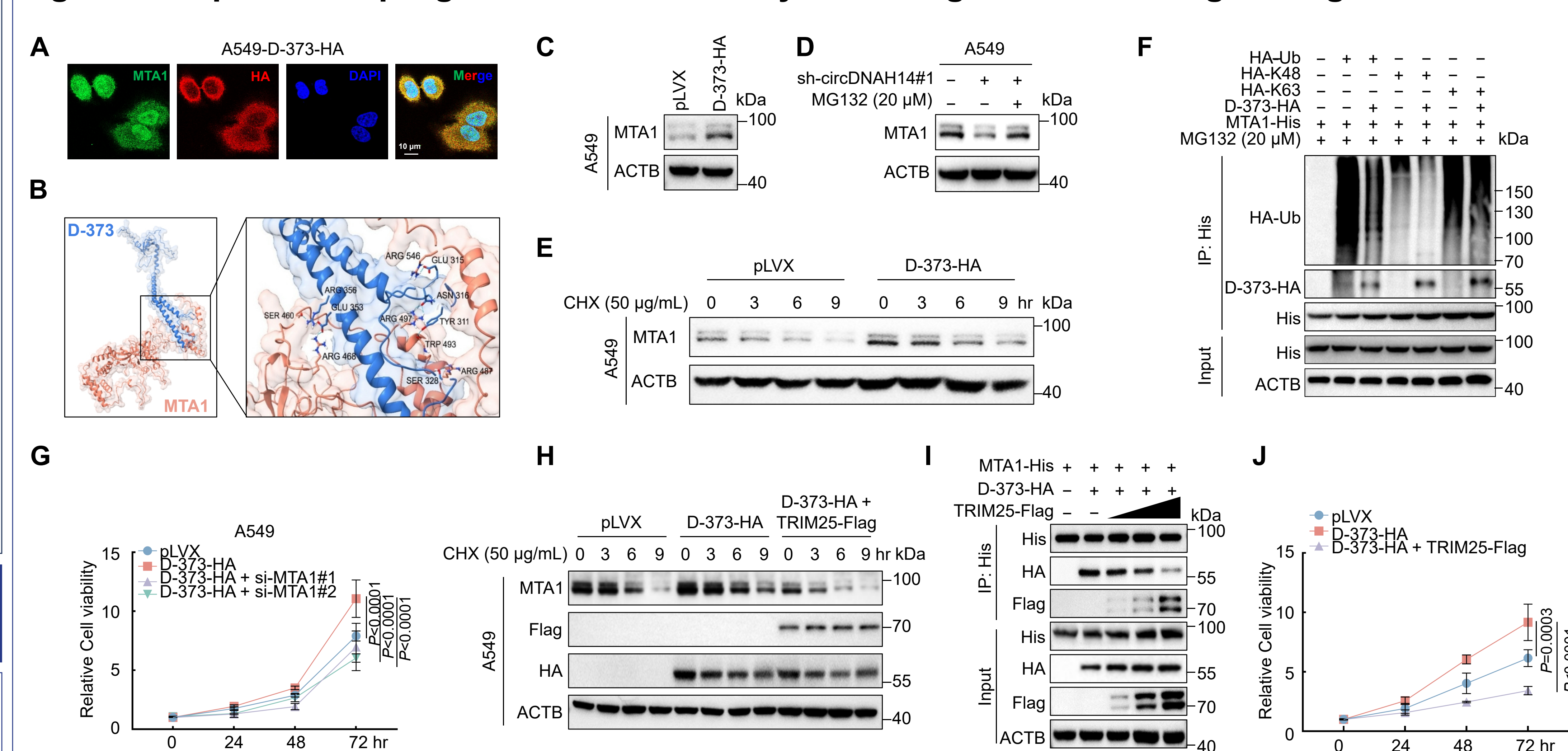


Fig.3 Teniposide directly targets D-373 to abolish its oncogenic function

