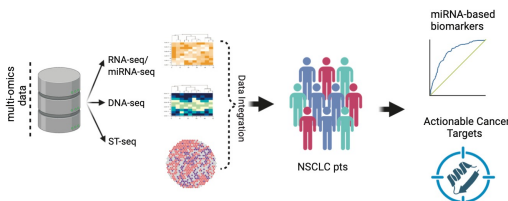
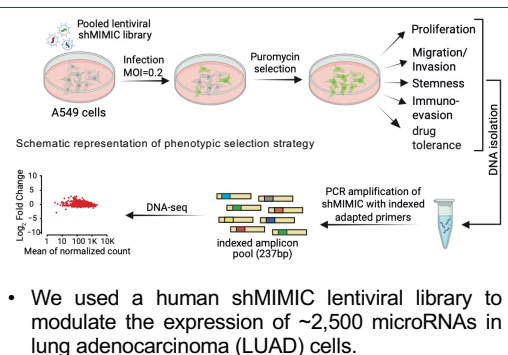


INTRODUCTION

Despite significant advances in understanding the biology of non-small cell lung cancer (NSCLC), key driver mechanisms remain incompletely characterized. Notably, a quarter of NSCLC cases lack identifiable oncogenic drivers. In addition, the molecular basis of resistance to chemotherapy and immunotherapy is still poorly understood. To address these gaps, we implemented a high-throughput functional screening strategy aimed at perturbing multiple molecular pathways by leveraging microRNAs, endogenous non-coding RNA of ~22 nucleotides, which play key regulatory roles in lung cancer-related mechanisms

METHODS



- We integrated shMIMIC screening data with multi-omics datasets and metadata from cohorts of NSCLC patients.

DISCUSSION AND CONCLUSION

- Here, we combined lentiviral shMIMIC screening with miRNA-seq/RNA-seq analysis of human LUAD samples including a large cohort of patients, and with Spatial Transcriptomics analysis, to systematically interrogate miRNAs and relative targets in NSCLC.
- This study provides a comprehensive functional and multi-omics characterization of the miRNome in NSCLC and identified new molecular axes that drive NSCLC progression, and mechanisms of immunoevasion.

REFERENCES & ACKNOWLEDGEMENTS

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- Cuttano R, J Hematol Oncol. 2022 Dec 31;15(1):178. doi: 10.1186/s13045-022-01394-1. PMID: 36587234

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Contact:



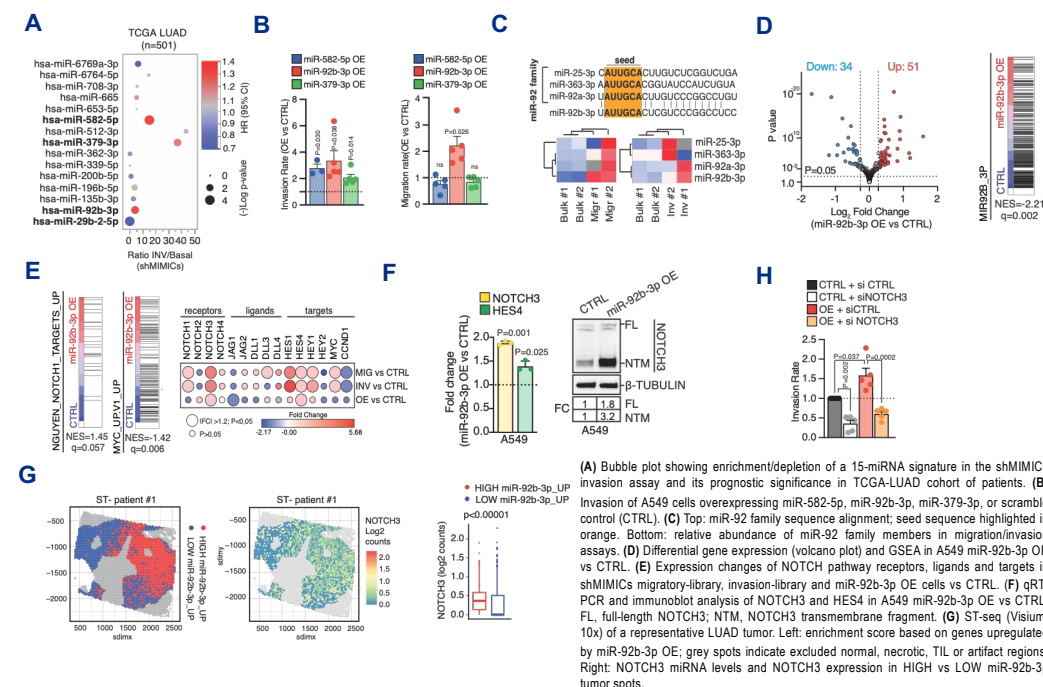
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Artificial Intelligence (AI) Use Disclaimer

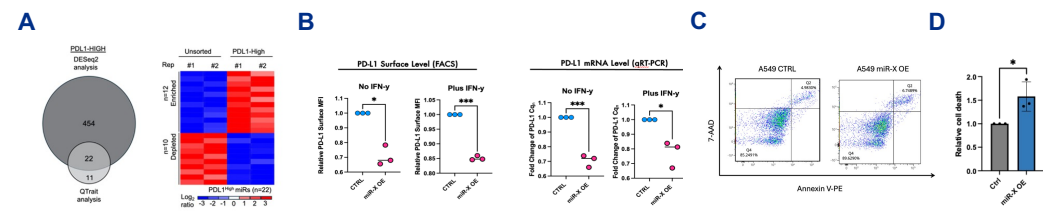
No AI based tools were used.

RESULTS

- Functional analysis of the human miRNome in NSCLC unveils a novel miR-92b-3p/NOTCH3 axis that drives tumor progression.**



- MicroRNA-Mediated Regulation of PD-L1 Drives Immune Evasion in NSCLC**



(A) Left panel: Venn diagram representing the overlap of miRNAs identified by shMIMIC screening in PDL1-High cells vs. unsorted by FACS, and using both DeSeq2 Analysis and qTrait analysis. **Right panel:** Heatmaps showing the relative abundance of miRNAs identified. Data are log2-ratio. **(B) Target validation (PD-L1):** of a selected candidate miRNA (miR-X) in the shMIMIC screening. **(C) FACS analysis:** of PD-L1 surface expression (left panel) and qRT-PCR (right panel) analysis of A549 lung adenocarcinoma cells overexpressing (OE) or not (CTRL) miR-X, treated by IFN γ or not to modulate PD-L1 expression. **(C-D)** A549 cells overexpressing (OE) or not (CTRL) the miR-X co-cultured with T-cells reveal increased tumour cell death following miRNA upregulation. * p<0.05, *** p<0.01.