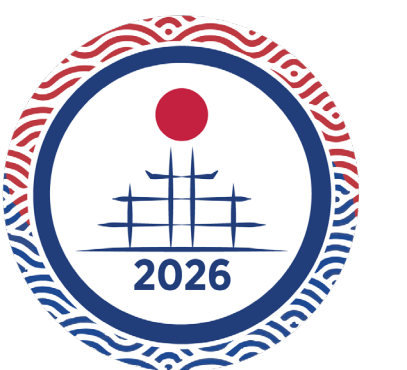




P1.292: Spatial exclusion of immune-evasive epithelial cells and CD8⁺ T cells in EGFR-mutant NSCLC with poor immunotherapy response

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INTRODUCTION

EGFR-mutant non-small cell lung cancer (NSCLC) often shows limited benefit from immunotherapy. However, the underlying molecular basis and spatial immune ecology remain unclear. We aimed to identify EGFR-associated molecular programs enriched in tumor epithelial cells and to evaluate their association with pathologic response to immunotherapy.

METHODS

Design: DepMap analysis identified an EGFR-mutant-specific 8-gene dependency signature through gene dependency and co-dependency analyses. Single-cell RNA-seq was used to characterize immune-evasive epithelial cells in MPR and NMPR tumors and evaluate signature activity. The signature was further validated in bulk RNA-seq. Spatial transcriptomics from 17 post-immunotherapy samples was used for spatial proximity analysis and GNN-based prediction of treatment response.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Actionable Take Away Message• An EGFR mutation-associated program enriched in immune-evasive epithelial cells is linked to CD8⁺ T-cell spatial exclusion and poor pathologic response in NSCLC.

Future Direction for Research

- The LGALS3–ALCAM axis may represent a potential biomarker and therapeutic target for improving response stratification and immunotherapy in EGFR-mutant NSCLC.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

- ◆ The EGFR-associated 8-gene signature was enriched in immune-evasive epithelial cells and significantly higher in NMPR than MPR tumors.
- ◆ Spatial transcriptomics revealed marked exclusion of CD8⁺ T cells from immune-evasive epithelial cells, enabling GNN-based response prediction (AUC: 0.917 training; 0.933 test).
- ◆ Cell–cell communication analysis implicated LGALS3 as a potential mediator of CD8⁺ T-cell exclusion.
- ◆ LGALS3 was associated with EGFR expression, and its knockdown reduced ALCAM, supporting a potential EGFR–LGALS3–ALCAM immune-evasion axis.

