



P1.275: Identification of Predictive Biomarkers for Immunotherapy Efficacy in Non-Small Cell Lung Cancer Based on Proteomics and Machine Learning

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INTRODUCTION

Immunotherapy is the core strategy for advanced NSCLC, but only a subset achieves durable clinical benefit with marked interindividual heterogeneity. Current biomarkers (PD-L1, TMB) are limited by tissue dependence, detection standardization issues, and restricted predictive performance, failing to meet clinical demands for precise treatment decisions. Developing non-invasive blood-based predictive biomarkers holds important translational value. This study aimed to identify a peripheral blood-based non-invasive biomarker to predict immunotherapy efficacy and prognosis in NSCLC patients.

METHODS

This study adopted a combined retrospective (public databases) and prospective design. NSCLC patients receiving immunotherapy were divided into the durable clinical benefit (DCB) group and no durable benefit (NDB) group, with 6-month progression-free survival (PFS) as the cutoff criterion for therapeutic efficacy. High-throughput proteomic sequencing was performed on 3 pairs of DCB/NDB baseline peripheral blood samples. Transcriptomic data from GSE72094 and GSE68465 were integrated with hundreds of machine learning algorithms were used to construct predictive models. Candidate genes from the optimal model underwent multivariate Cox regression, then intersected with differentially expressed genes to identify MMP19. GO, KEGG, CIBERSORT, and IPS analyses were used for functional and immune infiltration evaluation. Finally, 50 immunotherapy-treated NSCLC patients were prospectively enrolled; ELISA detected baseline target gene protein levels to verify predictive value for efficacy and prognosis.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- MMP19 is a non-invasive, independent adverse predictor of NSCLC immunotherapy response (HR = 2.457).
- Low baseline MMP19 protein levels are associated with durable clinical benefit (DCB), whereas high MMP19 predicts significantly poorer OS, enabling pretreatment patient stratification.
- MMP19 reshapes the immune microenvironment.

Future Direction for Research

- Validate in larger multicenter cohorts with standardized ELISA cutoffs.
- Explore MMP19 inhibition as a strategy to sensitize immunotherapy.
- Combine MMP19 with more other markers to improve prediction models.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

- StepCox[forward] + RSF model achieved optimal predictive performance. Six candidate genes were screened, and **MMP19** was identified as the key target after intersection with differentially expressed genes and multivariate Cox regression.
- MMP19 expression correlated positively with M2 macrophages and neutrophils (p<0.05), and negatively with plasma cells, M1 macrophages, and NK cells. High MMP19 was associated with significantly lower immunophenoscore (IPS) (p<0.05).
- In 50 prospectively enrolled NSCLC patients, DCB patients had significantly lower baseline MMP19 protein levels than NDB patients (p<0.05, ELISA).
- High MMP19 expression predicted significantly poorer OS. Multivariate Cox regression confirmed MMP19 as an independent prognostic risk factor (**HR=2.457, 95%CI: 1.010–5.979, p<0.05**).

