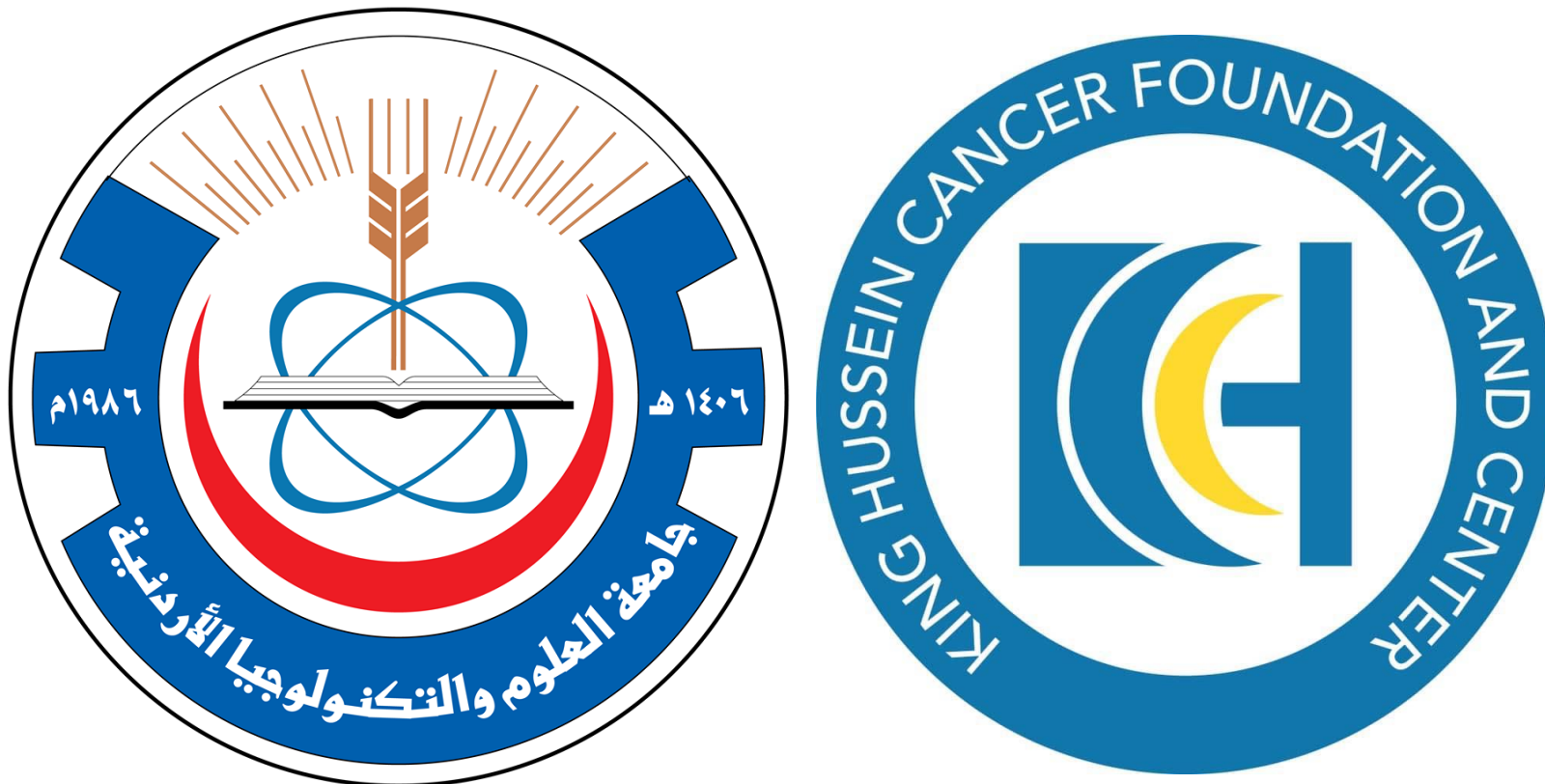




INTRODUCTION

- **NSCLC** is strongly associated with smoking and remains a leading cause of cancer-related mortality worldwide.
- **EMT** plays a key role in tumor progression and metastasis.
- The **smoking-related EMT transcriptional profile** and its prognostic significance in NSCLC remain poorly understood.
- **Aim:** To identify an **EMT-related gene signature associated with smoking status** in NSCLC and evaluate its **prognostic value**.

METHODS

- **Study population:** 450 NSCLC patients from TCGA (382 ever-smokers, 68 never-smokers)
- **Differential expression analysis:**
 - DESeq2 was used to identify DEGs
 - Criteria: adjusted $p < 0.05$ and $|\log_2FC| > 0.9$
- **EMT gene selection:**
 - EMT-related genes were obtained from **MSigDB**
 - DEGs were intersected with EMT-related genes to identify EMT-DEGs
- **Prognostic gene selection:**
 - LASSO Cox regression was performed to reduce overfitting
 - Univariate and multivariate Cox regression identified independent prognostic EMT-DEGs
- **Risk score construction:**
 - Calculated using multivariate Cox regression coefficients
 - Patients were divided into **high- and low-risk groups** using the median cutoff
- **Survival analysis:**
 - Kaplan-Meier survival curves, Log-rank tests, Time-dependent ROC/AUC analysis to assess predictive performance
- **Immune analysis:**
 - Immune cell infiltration was estimated using **quanTlseq**
 - Wilcoxon rank-sum tests were used to compare immune gene expression and immune-cell infiltration between risk groups
- **External validation:** using **GEO dataset GSE50081**

DISCUSSION AND CONCLUSION

- An EMT-based risk score successfully stratified NSCLC smokers into high- and low-risk groups with significantly different survival outcomes.
- Low-risk patients showed **higher expression of immune checkpoint markers**, including CTLA4, and greater M2 macrophage infiltration.
- These findings **suggest distinct immune microenvironment** profiles between risk groups.
- The EMT-based signature highlights the interplay between tumor progression and the immune microenvironment.
- These findings may inform potential therapeutic targets and personalized treatment strategies in NSCLC smokers.

REFERENCES & ACKNOWLEDGEMENTS

Artificial Intelligence (AI) Use Disclosure: No artificial intelligence tools were used in the development of this poster.

RESULTS

4,290 significant DEGs were identified.

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Intersection with EMT-related genes yielded **192 EMT-DEGs**.

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LASSO regression narrowed these to **20 genes**.

↓

Cox analysis identified 5 genes significantly associated with patient outcomes: **DHRS2**: HR = 1.240, **ATP10B**: HR = 0.855, **MYT1**: HR = 0.796, **UGT2B15**: HR = 0.866, **LINC01133**: HR = 1.144

↓

An **EMT-based risk score** was constructed using these 5 genes, with patients classified into high- and low-risk groups using the median cutoff: **High-risk patients had significantly worse OS** than low-risk patients (**log-rank $p < 0.001$**).

↓

The model showed strong predictive performance:
1-year AUC: 0.79, 3-year AUC: 0.80, 5-year AUC: 0.78
Low-risk patients had significantly higher expression of:
TOX: $p = 0.0003$, **EOMES**: $p = 0.02$, **CTLA4**: $p = 0.041$.
PDCD1, TIGIT, CD274, and LAG3 showed no significant differences (**$p > 0.05$**).

↓

M2 macrophage infiltration was significantly higher in low-risk patients (**$p < 0.05$**).

↓

In an independent cohort of **136 NSCLC smokers**, the same cutoff similarly identified **high-risk patients with poorer OS**.