



P3.339: Aberrantly Exonized Transposable Elements Predict Immunotherapy Benefit in Small Cell Lung Cancer

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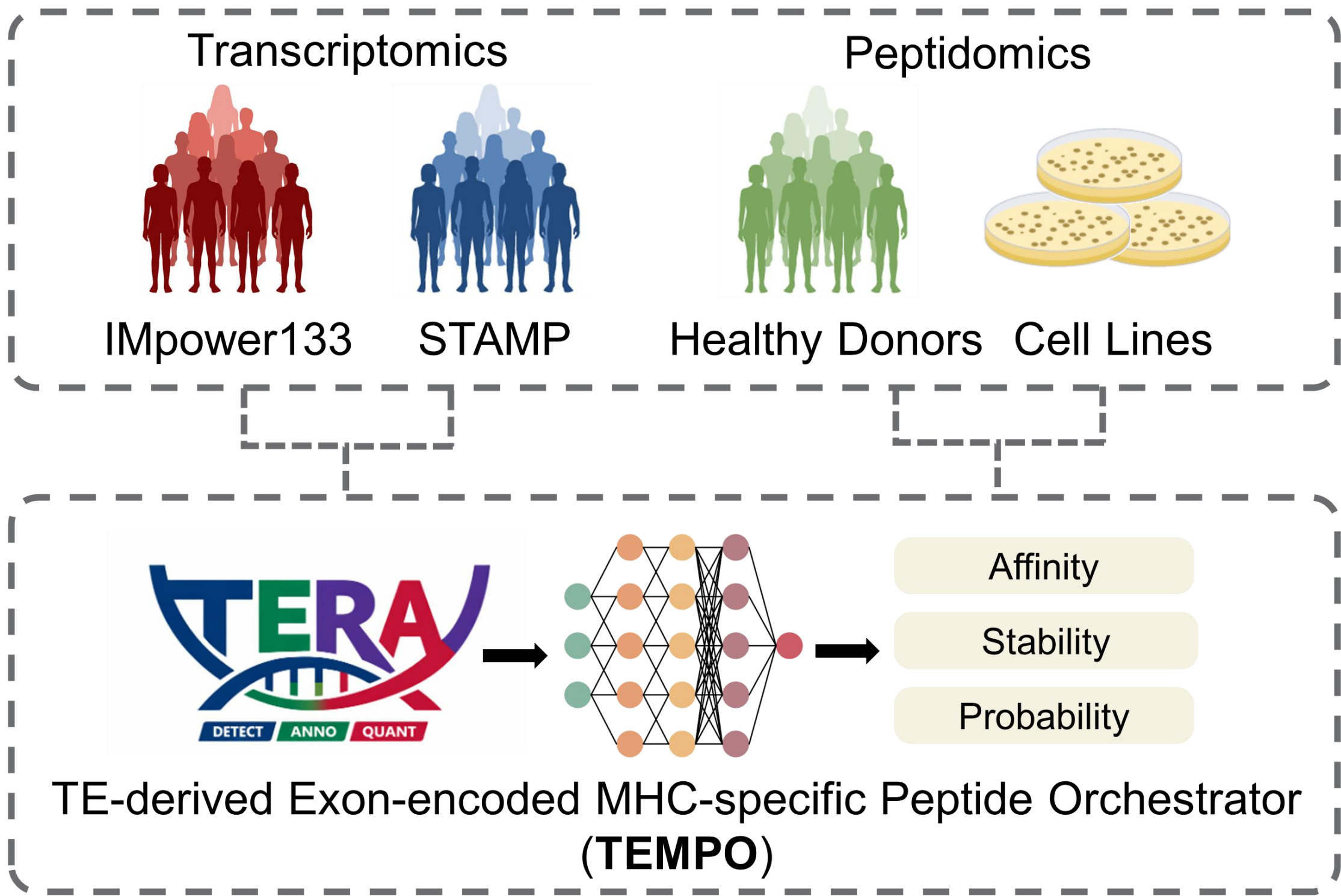
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INTRODUCTION

Small cell lung cancer (SCLC) is hallmarked by concurrent TP53 and RB1 mutations, triggering epigenetic dysregulation and subsequent massive exonization of transposable elements (TEs). Although aberrantly exonized TEs have been reported to encode novel antigens and predict immune checkpoint blockade (ICB) efficacy in various malignancies, their role in SCLC remain unexplored.

METHODS

TE-exon-encoded immunopeptides were identified by applying our in-house TEIPS pipeline to the IMpower133 and in-house STAMP cohorts. Survival analysis was performed using the IMpower133 cohort, and the immunogenicity of the identified peptides was validated by ELISPOT assays.

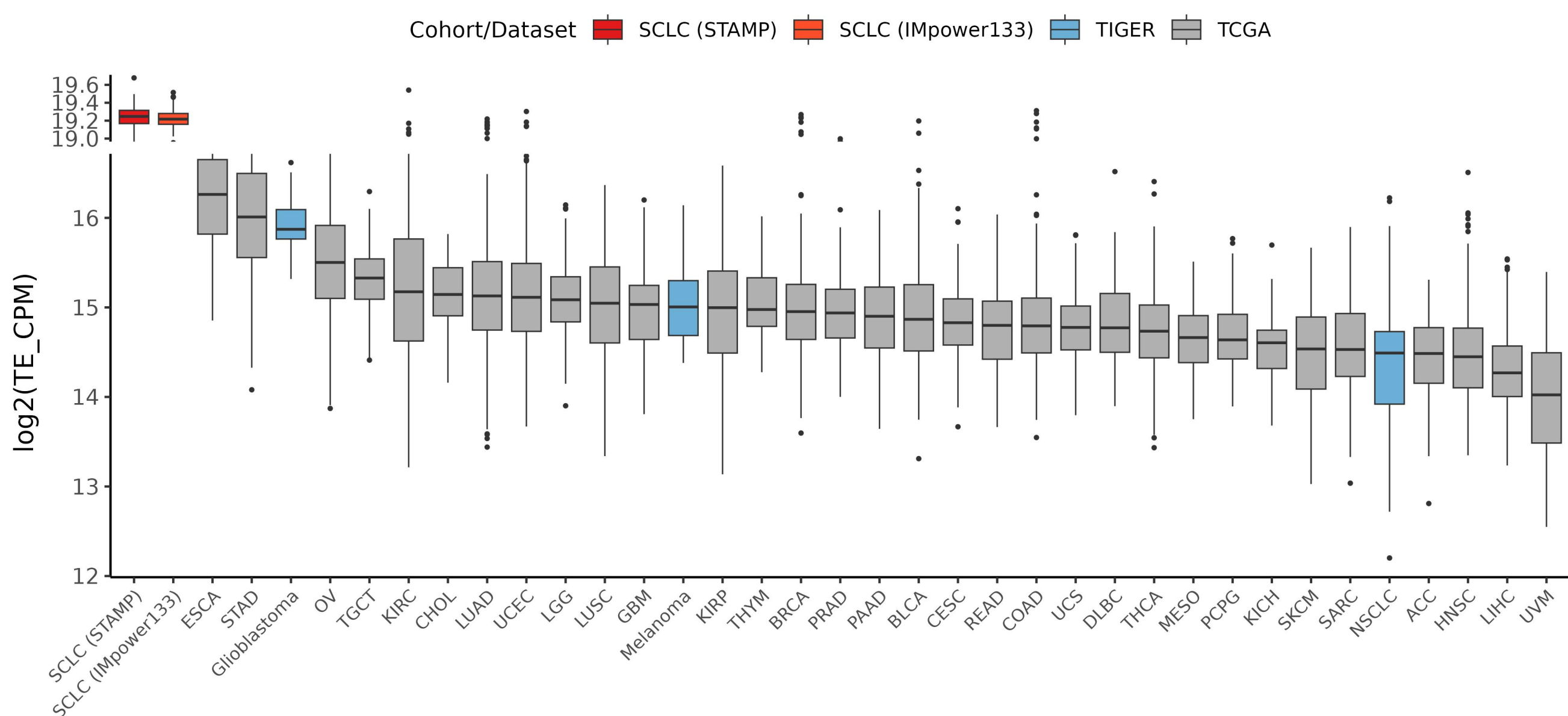


REFERENCES & ACKNOWLEDGEMENTS

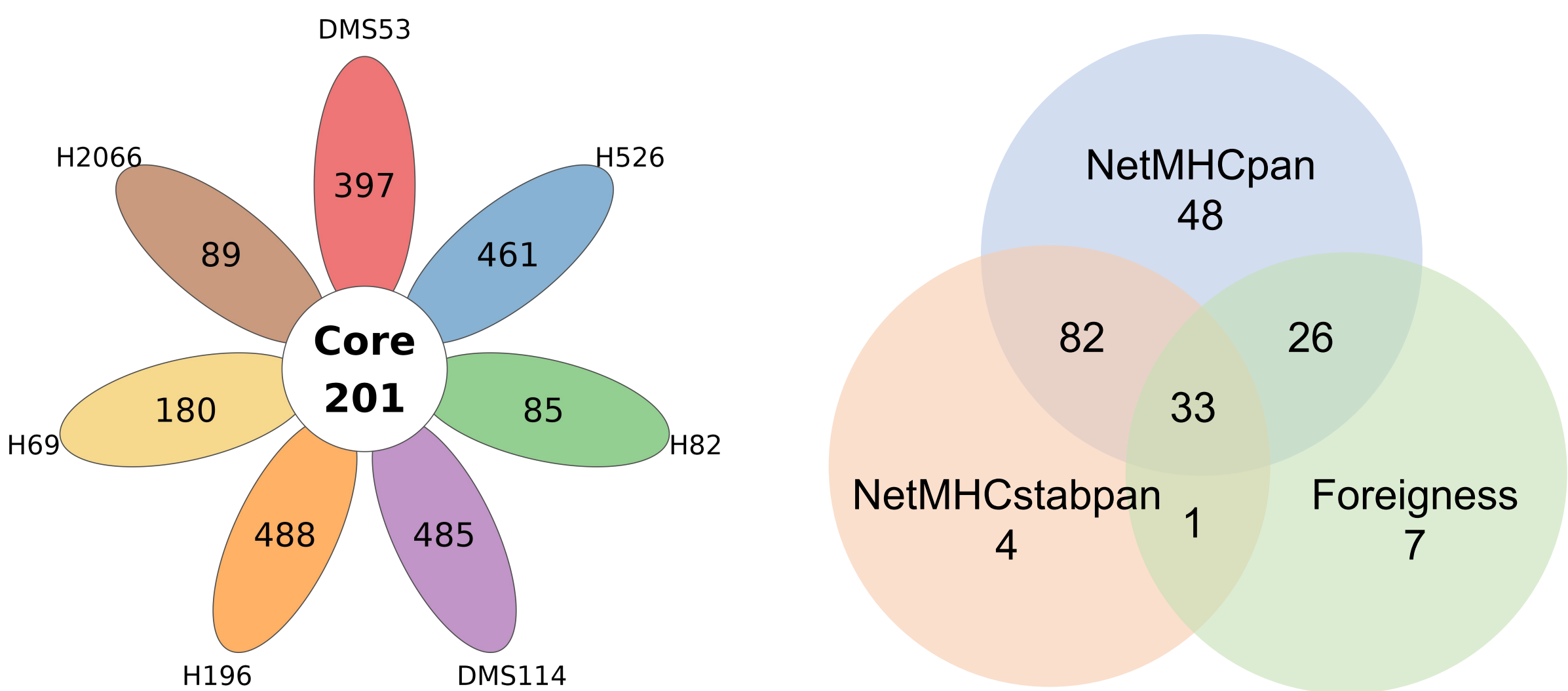
- The authors declare no conflicts of interest related to this work.
- In compliance with ACCME standards, we confirm that no artificial intelligence tools were utilized in the development or content creation of this poster.

RESULTS

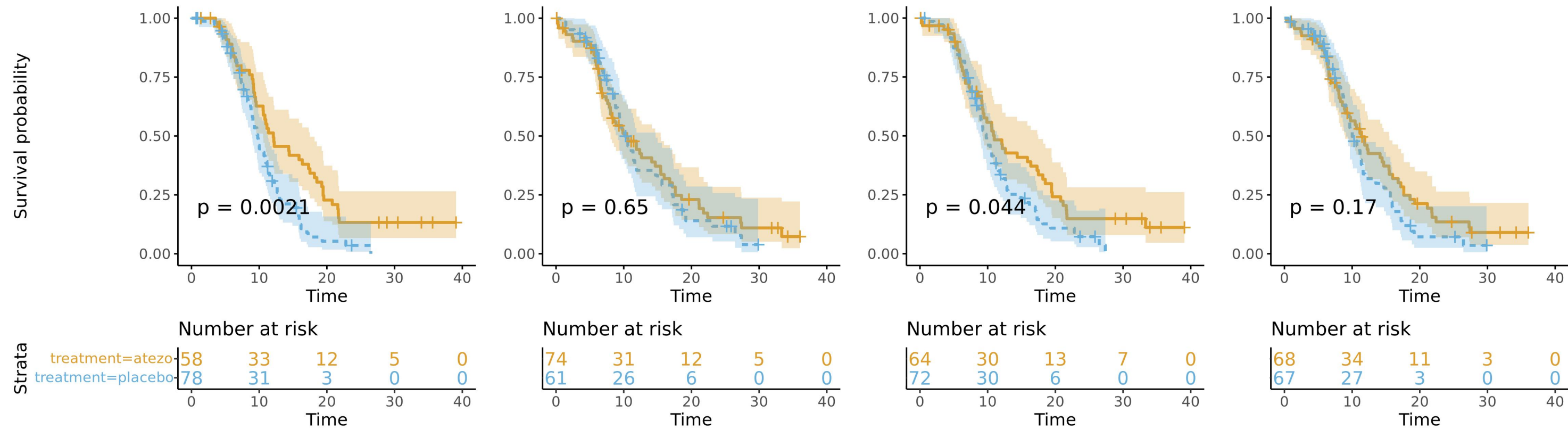
A. Pan-cancer analysis identified SCLC as the tumor type with the highest overall TE expression.



B. TEIPS identified TE-exon-encoded immunopeptides. Left panel: TERA and TIPs detected 201 tumor-specific TE-exon-encoded peptides presented by HLA in ≥2 SCLC cell lines. Right panel: NetMHCpan, NetMHCstabpan, and Foreignness prioritized 33 peptides predicted to bind strongly to HLA and be immunogenic.

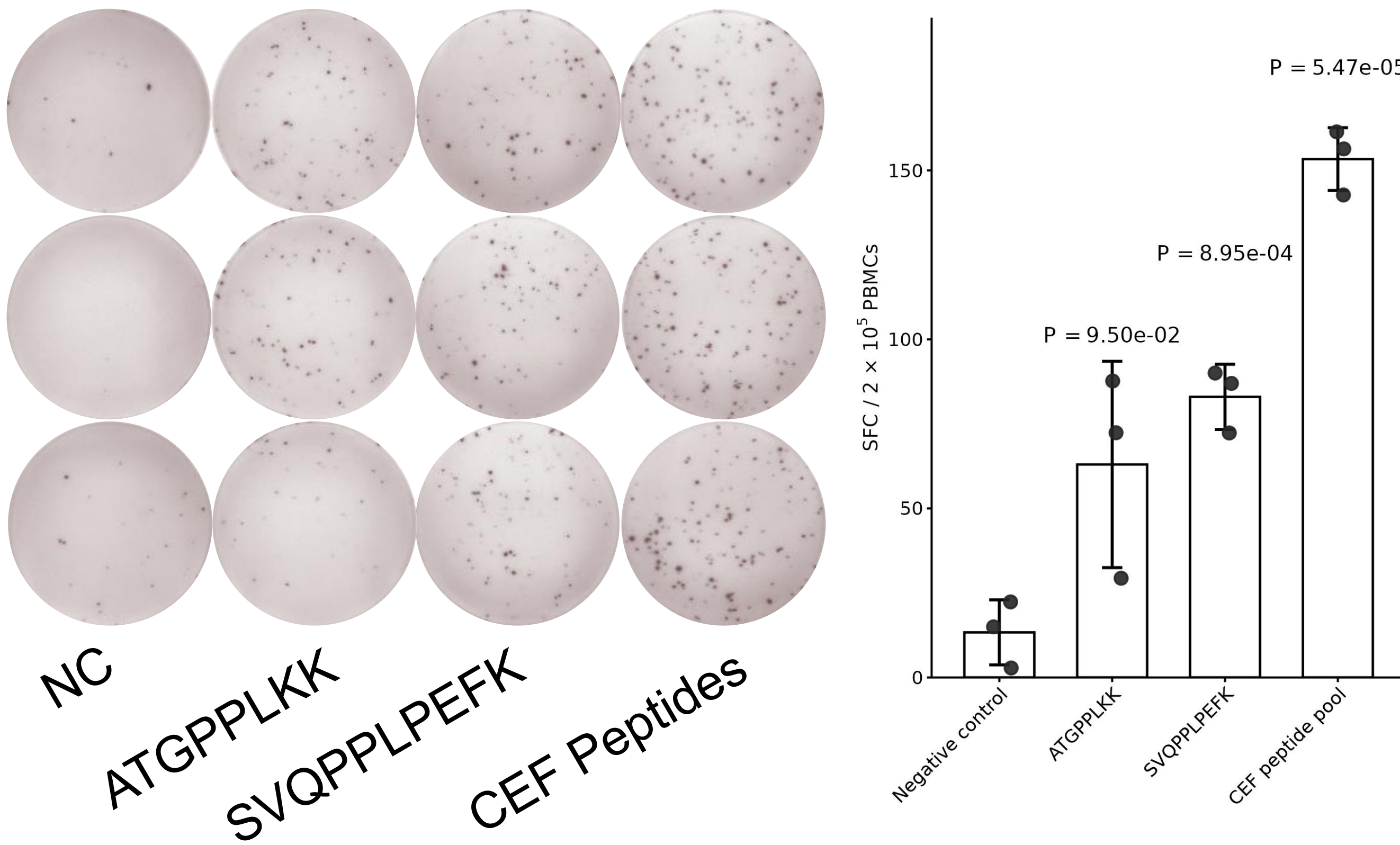


C. Bootstrapping analysis of IMpower133 revealed peptide-encoding TE-exons of predictive value. High expression of two candidate peptide-encoding TE-exons was associated with prolonged OS under atezolizumab versus placebo.



TEExon-ATGPPLKK Expression: High vs. Low
TEExon-SVQPPLPEFK Expression: High vs. Low

D. ELISPOT assays confirmed the immunogenicity of the selected peptides.



DISCUSSION AND CONCLUSION

- This study identifies aberrantly exonized transposable elements as a source of tumor-specific novel proteins in SCLC, and high expression of candidate TE-exons serves as a biomarker for predicting prolonged OS with atezolizumab.
- Coupled with their absence in normal tissues, these findings highlight aberrantly expressed TEs as both predictive biomarkers for ICB benefit and candidate targets for future antigen-directed immunotherapies.