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INTRODUCTION

- Immune checkpoint blockade (ICB) has achieved success in many cancers.
- Checkpoint-induced pneumonitis (CIP) and efficacy improvement represent two main challenges in ICB.
- Strategies to prevent CIP while synergistically enhancing ICB efficacy are clinically needed.

METHODS

- Multi-omics analysis including single-cell RNA sequencing of PBMC and BALF, bulk transcriptomic, and clinical efficacy and toxicity data.
- Conditional gene knockout (cKO) mice undergoing radiation-based ICB lung injury.
- In vivo cell tracing by fluorescence labeling and imaging.
- In vitro T helper cell polarization assays.
- In vitro chemotaxis and activation assays.
- In vivo vaccination plus ICB and pneumonitis testing assays.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- TNFSF8+CD4⁺T cells drive CIP via CD30-TNFSF8-induced ADGRE5-SFTPD interaction.
- CCL3-CCR1 axis-mediated neutrophil chemotaxis and IL-17-mediated Neu degranulation injure lung tissue.
- TNFSF8-CpG vaccine may be a transformative preventive way for CIP and ICB efficacy improvement.

Future Direction for Research

- Humanized vaccine developments and efficacy and safety validation.
- Cohorts-based validation of blood biopsy of TNFSF8⁺CD4⁺T cells across different time points.

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RESULTS

