



P2.012: Small-Molecule Inhibitor KIRA6 Reverses Immunotherapy Hyperprogression Induced by SRSF9 Overexpression in Tumors

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INTRODUCTION

- Hyperprogressive disease (HPD) is a severe pattern of accelerated tumor progression after immunotherapy.[1,2]
- Reliable biomarkers and effective targeted therapies for HPD remain lacking.[2]
- We aimed to identify key HPD regulators, define their spatial immune mechanisms, and explore therapeutic strategies.

METHODS

Design:

- Integrated single-cell RNA sequencing data from HPD and non-HPD tumors with TCGA analysis to identify candidate regulators.
- Validated the clinical relevance of key candidates in an independent patient cohort.
- Applied spatial protein cytometry by fluorescence (PCF) to characterize cellular neighborhoods and spatial interactions.
- Screened a 106,100-compound library and evaluated candidate binding using BLI and SPR.
- Assessed therapeutic efficacy in Srsf9-overexpressing LLC1 tumor models.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- SRSF9 is a key regulator of HPD** and is associated with poor clinical outcomes.
- KIRA6 combined with immunotherapy reverses HPD-related tumor progression**, supporting SRSF9 as a potential therapeutic target.

Future Direction for Research

- Validate **SRSF9** as a **predictive biomarker** for HPD.
- Further assess the **mechanism and translational potential of KIRA6** in immunotherapy-associated HPD.

REFERENCES & ACKNOWLEDGEMENTS

References

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Artificial Intelligence (AI) Use Disclaimer

DeepSeek was used solely for English language polishing, grammar correction, and stylistic refinement.

No AI tools were used for experimental design, data collection, data analysis, result interpretation, or generation of core scientific content.

RESULTS

