Novel TCRs against mutated KRAS, NRAS, and androgen receptor, and TCRs identification platform

Therapeutics

Reference Number: **1926** \ Principal Investigator: **Prof. Yardena Samuels**
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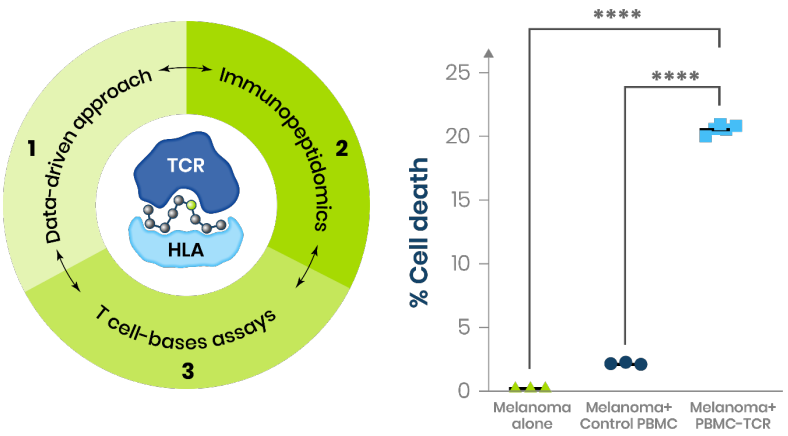
Immunotherapy can induce durable tumor regression in patients with metastatic cancer, largely driven by the immune system's recognition of tumor-specific neoantigens. We developed a robust, high-throughput platform for the identification and biological validation of HLA class I and II recurrent immunogenic neoantigens and their corresponding TCRs.
Leveraging this platform, we successfully identified and validated a suite of TCRs targeting clinically relevant neoantigens—including those derived from hotspot mutations in NRAS, PIK3CA KRAS, HRAS, and the androgen receptor—enabling the development of TCR-based therapies for a broad range of solid tumors.



Engineered T cells expressing NRAS-specific TCR effectively eliminate neoantigen-expressing melanoma cells

APPLICATIONS

- Discovery and validation of TCRs against common immunogenic neoantigens
- Off-the-shelf TCR cell therapy for cancer patients
- Extension to microbial, viral, or autoimmune diseases
- Neoantigen mRNA-based vaccines

DEVELOPMENT STAGE

- Pipeline of TCRs ready for clinical trials targeting NRAS (Q61K), NRAS (Q61R), KRAS (Q61K), KRAS (G12V), KRAS (G12C), HRAS (Q61K), Androgen Receptor (H875Y).
- Additional TCRs in the discovery and validation stages

DIFFERENTIATION

Discovery of common and highly immunogenic neoantigens

Robust TCRs biological validation

Identification of both HLA class I and class II neoantigens

TCRs with a higher probability of clinical success

REFERENCES

- Peri et al., J Clin Invest, 2021
- Gumpert et al, Cener Discov, 2025
- Sagie et al, Cell Rep Med., 2025

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