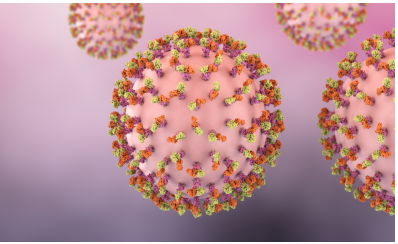
Biomarker-guided selection of potent tumor-specific TCRs

T cells are central to anti-tumor immunity, but only a minority of tumor-specific TCRs provides strong and durable protection. Today, finding such high-functionality TCRs requires complex functional screens and often invasive tumor sampling. A robust, blood-based way to pinpoint the most protective TCRs would significantly accelerate development, de-risk selection and reduce cost of personalized T cell therapies and related diagnostics.

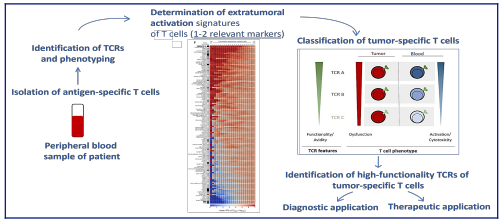


PD-1–based enrichment of high-affinity tumor TCRs

IP RIGHTS
PCT filed, US and EP pending
2023

The technology decodes a "success signature" of tumor-specific T cells: high PD-1 surface levels plus defined activation-gene expression in peripheral blood reliably mark TCRs with superior functional avidity. This enables targeted isolation, ranking and engineering of the most potent tumor-reactive TCRs without TILs or labor-intensive empirical screening.

01 Easy, cost-efficient enrichment of highly functional tumor-specific TCRs from peripheral blood
02 PD-1 and activation-gene markers as a biomarker panel for TCR discovery assays
03 Applicable to T-cell therapy development and diagnostics
04 Broadly applicable across solid tumors and adaptable to diverse neoantigen targets



Extratumoral activation signatures serve as a biomarker for identification of high-functionality TCRs of tumor-specific T cells

CHALLENGE

Tumor antigen-specific T cells are central to cancer control and are already exploited in TCR-engineered T-cell therapies and TIL products. However, only a fraction of tumor-reactive TCRs are truly protective. Because the TCR repertoire is highly dynamic across tissues and over time, and functional avidity is difficult to measure, identifying high-functionality TCRs remains complex, resource-intensive and a key bottleneck for therapeutic and diagnostic development.

INNOVATION

The invention provides a biomarker-based system to identify highly functional tumor-specific TCRs directly from peripheral blood. Single-cell sequencing of neoantigen-specific T cells combined with CRISPR-Cas9 TCR reexpression shows that TCRs with superior protective capacity are enriched in T cells with signatures of recent activation. PD-1 surface expression and defined activation-gene markers form a practical, scalable framework to enrich, rank and prioritize such TCRs for therapeutic and diagnostic use.

01 Basic principles observed · **02** Technology concept formulated · **03** Experimental proof of concept · **04** Technology validated in lab · **05** Technology validated in relevant environment · **06** Technology demonstrated in relevant environment · **07** System prototype demonstrated in operational environment · **08** System complete and qualified

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