Docket #: S24-100

Engineered transcription factors to enhance T cell function in cancer immunotherapy

Stanford scientists have developed engineered transcription factors that enhance T cell function and prevent exhaustion by systematically combining functional protein domains. Through targeted control of cell state, these synthetic factors demonstrate improved capacity to maintain T cell function under chronic antigen exposure. This systematic engineering approach to transcription factors could significantly advance cellular engineering across therapeutic applications, including cancer immunotherapy and regenerative medicine.

Enhancing T cell function for cancer immunotherapy has traditionally relied on manipulating endogenous genes through knockouts or overexpression of natural transcription factors. However, these approaches often result in limited or suboptimal T cell responses, particularly in challenging solid tumor environments where T cells face persistent antigen exposure and immunosuppressive conditions. Current engineering methods are constrained by the inherent limitations of endogenous transcription factors, which have evolved for normal physiological functions rather than therapeutic applications. The development of more effective cellular engineering approaches that can drive sustained T cell responses in therapeutic contexts represents a critical need in the field of cancer immunotherapy.

Testing of a library of ~8,000 synthetic transcription factors in multiple human T cell donors revealed several novel variants that substantially improve T cell function under chronic antigen exposure conditions. Notably, many of these engineered transcription factors outperformed natural transcription factors in enhancing T cell function, establishing a diverse set of effective tools for cellular engineering. This systematic approach to engineering synthetic transcription factors shows promise for enhancing cellular engineering in cancer immunotherapy and could provide a

valuable platform for optimizing cell function across diverse therapeutic applications.

Stage of Development:
Proof of concept
Continued research – Validation of hits in in vitro T cell assays and applying the synthetic transcription factors in stem cell models

If interested in this technology, please reach out to us by March 30, 2025.

Applications

- Engineering of T cells for improved cancer immunotherapy
- Optimization of cellular engineering across therapeutic applications
- Cellular state modification for regenerative medicine

Advantages

- Systematic approach to generating effective transcription factors
- Library of diverse synthetic transcription factors with demonstrated efficacy
- Versatile engineering platform adaptable to different cell types
- Robust performance across multiple donor genetic backgrounds

Innovators

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