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Synthetic Erythroblast Transformation Specific (ETS) Transcription Factors for Cellular Engineering

Stanford researchers have developed a high-throughput platform to engineer synthetic ETS transcription factors that enhance human T cell function beyond natural TFs, enabling precise and scalable cellular reprogramming for immunotherapy and other therapies.

Traditional methods for engineering human cells, such as gene knockouts or overexpressing natural transcription factors (TFs), offer only limited control over cell behavior. These approaches often fail short in producing the robust and functional cell states required for effective therapies, particularly in challenging environments like solid tumors, where T cells become exhausted and lose their ability to fight cancer.

To address these limitations, Stanford researchers have created a scalable, high-throughput platform for cellular reprogramming using Synthetic Erythroblast Transformation Specific (ETS) transcription factors. By leveraging CRISPR-All technology, the team built and screened a library of ~8,000 synthetic ETS TFs in human T cells under chronic antigen exposure. Several synthetic TFs were identified that significantly outperformed their natural counterparts in restoring and enhancing T cell function, offering a powerful and versatile tool for precise cellular reprogramming in therapeutic settings.

Stage of Development:
Research - in vitro.

Applications

- Cancer immunotherapy
- Regenerative medicine
- Drug discovery
- Synthetic biology

Advantages

- Superior functional impact and greater control over cellular behavior
- Increased design flexibility
- Scalable platform
- Broad biological utility

Innovators

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