

Cell & Gene Therapies – TCRs and CARs for T-Cell-Based Immunotherapies

The Platform

Since treatment options for many diseases including cancer and chronic infections are still limited, many patients do not receive adequate therapy. Adoptive transfer of genetically engineered T-cells has shown promise for the treatment of such diseases in recent clinical studies. The immunotherapy approach aims at helping the patient's own immune system to defend the body against diseased cells by utilizing either antigen-specific T-cell receptors (TCRs) or chimeric antigen receptors (CARs). The lack of suitable receptor candidates, however, has been

a major limitation of these treatment strategies in the past. To this end, we have developed a platform technology for high-throughput cloning and characterization of naturally selected TCRs. Our CAR and TCR platform is fast and flexible and allows for TCR isolation from single T lymphocytes of patient samples in as little as 11 days. With these features, the platform has the potential to become a mainstream tool for truly personalized and broadly applicable targeted immunotherapies.

The Science

We are using our proprietary high-throughput platform for the fast isolation of antigen-specific T-cells, efficient cloning and rapid validation of novel antigen-specific T-cell receptors and epitopes on the basis of single antigen-reactive T lymphocytes. The TCRs currently available for clinical use are restricted to a few well-characterized (tumor) antigens and to the most common HLA (Human Leukocyte Antigen) presented epitopes. In contrast, our approach facilitates the generation of large libraries of TCRs against multiple antigens and various HLA types. Receptor

candidates are further improved using our extensive knowledge of molecular biology, immunogenetics and T-cell immunology. Our portfolio of antigen-specific immune receptors is constantly growing. Our main focus currently lies on TCRs and CARs directed against cancer antigens that are selectively expressed by tumor cells. We also aim to progress promising lead candidates into preclinical and clinical development to develop highly potent immunotherapies with excellent safety profiles.

Our Vision

... is to make our platform a standard tool for the development of targeted immunotherapies.

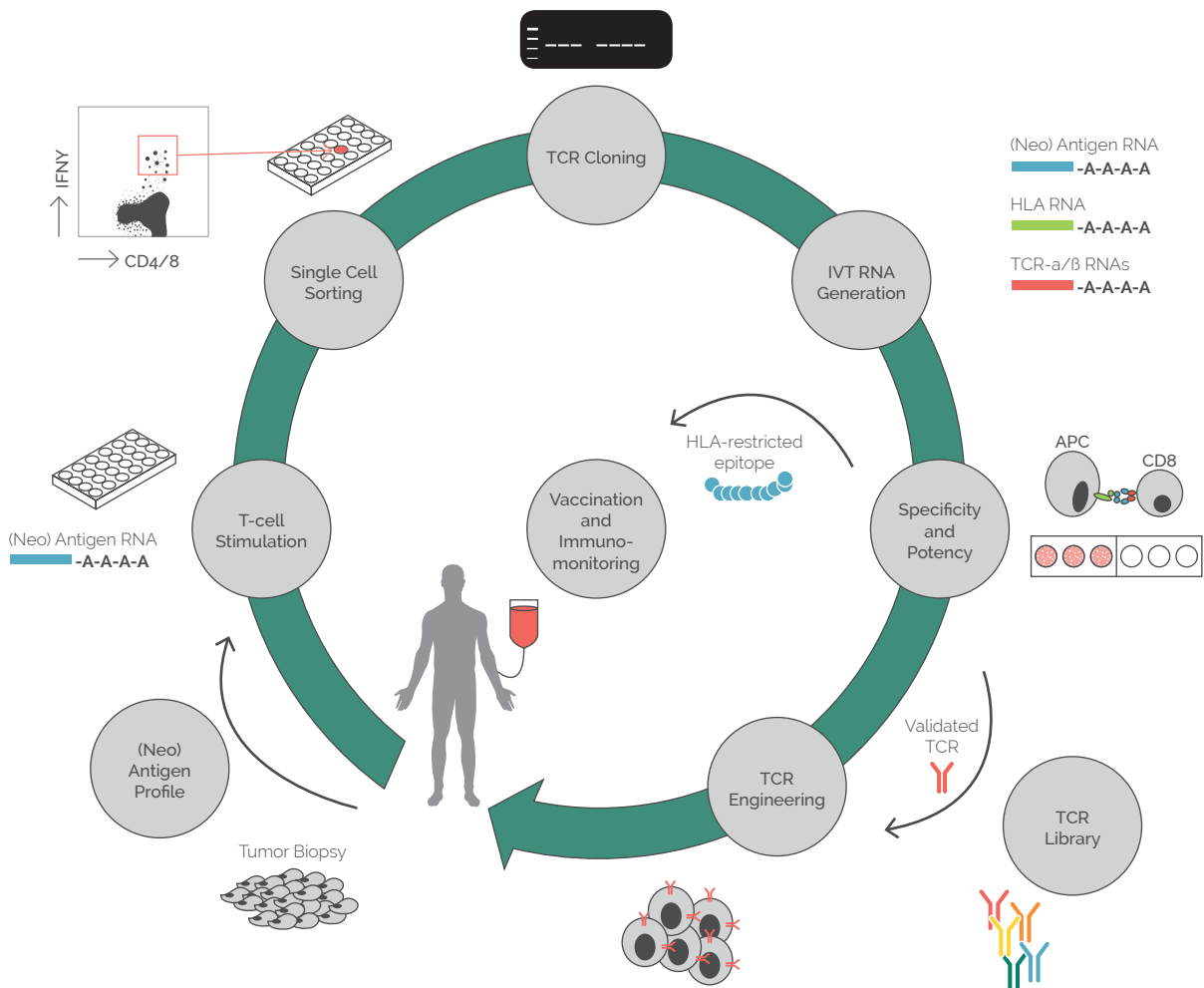
... is to use our platform for the development of better, highly efficacious and safe immunotherapies.

- Stratified approaches: Identification of single TCRs against defined antigen/HLA combinations derived from shared tumor antigens.
- Personalized "off-the-shelf" therapy: Generation of a warehouse of immune receptors for "off-the-shelf" use to match each individual patient's tumor and HLA haplotype and to target two or more antigens simultaneously.
- Truly personalized T-cell therapy: On-demand and timely manufacturing of customized, engineered T-cells with autologous TCRs against neo-epitopes for adoptive transfer.

Our Evidence

We have a vast and diversified portfolio of immune receptor candidates:

- More than 160 functionally validated TCRs against 20 different oncology targets.
- More than 60 different T-cell epitopes identified.



We are in preclinical development with our lead candidate, a CAR that targets an antigen frequently expressed in ovarian, endometrial and lung cancers. Clinical testing is expected to start in 2017.