Rapid Generation of Single-Chain Antibodies for Use as Chimeric Antigen Receptors (CARs)

Rapid and efficient identification of high-affinity, antigen-specific single-chain antibodies for the construction of chimeric antigen receptors (CARs) to improve the effectiveness of CAR T-cell therapies, particularly in targeting challenging cancer antigens.

Technology

This technology leverages a novel genetically engineered mouse model to rapidly generate single-chain antibodies (Abs) for use in creating heavy chain-only Abs (HCAbs). These HCAbs can be utilized to develop CAR libraries, which are expressed in primary T cells and screened using single-cell functional assays. This method enables the rapid identification of CAR clones with optimal binding properties, offering a promising approach to enhance CAR T-cell therapies by targeting challenging cancer antigens with high specificity.

Background

Traditional methods for generating single-chain antibodies often involve labor-intensive processes, such as phage display and hybridoma technology, which may not provide the necessary affinity and specificity for targeting transmembrane and intracellular cancer antigens. This technology addresses these limitations by using a murine model designed to facilitate *in vivo* affinity maturation, producing high-affinity antibodies with greater specificity. The Koralov and Yarmarkovich labs have developed this platform to overcome the challenges associated with traditional antibody generation methods, offering a more direct and efficient path from antigen identification to therapeutic development.

Development Stage

The technology is currently in the preclinical stage, with ongoing validation and optimization efforts in the Koralov and Yarmarkovich labs. Preliminary data demonstrate the platform's potential to generate high-affinity CAR T-cell constructs with specificity for challenging tumor antigens.

Applications

- Development of next-generation CAR T-cell therapies targeting oncogenic transmembrane and intracellular antigens
- Rapid generation of antibody libraries for therapeutic applications in oncology
- Screening and identification of high-affinity, antigen-specific CAR clones for personalized cancer treatments

Technology ID

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Category

Life Sciences/Platform Technology
Life Sciences/Genetic Engineering
Life Sciences/Research tools/Oncology
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Advantages

- Eliminates the need for immunizing camelids, simplifying the conventional single-chain antibody generation process, making it more efficient and less resource-intensive
- Eliminates the need for time-consuming phage display libraries and hybridoma technology, allowing for faster development of CAR T-cell therapies with higher specificity, affinity, and reduced off-target effects
- Utilizes a genetically engineered mouse model that mimics the natural antibody development process, improving the likelihood of identifying therapeutic candidates with superior binding properties in a high-throughput manner
- Bypasses the need for heavy-light chain antibody pairing, streamlining the generation of CAR libraries
- Allows for compatibility with a broader range of antigens, including transmembrane and intracellular antigens
- Accelerates the timeline from discovery to therapeutic application of CAR T-cells

Intellectual Property

Provisional patent application pending.