

## **Abstract: Novel tools to improve T cell therapies for cancer**

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Adoptive T cell therapies have transformed the treatment landscape for hematological malignancies and are increasingly being explored for solid tumors and personalized cancer treatment. Realizing the full potential of these therapies requires innovation across the entire development pipeline, from identification of highly specific tumor-targeting receptors to manufacturing approaches that preserve T cell functionality and persistence.

In this seminar, I will present recent advances aimed at overcoming key bottlenecks in T cell engineering. First, I will describe how state-of-the-art generative artificial intelligence and protein design technologies can be leveraged to create de novo minibinders that recognize peptide-major histocompatibility complex (pMHC) targets associated with cancer. These engineered binders can be incorporated into chimeric antigen receptors to direct potent antigen-specific tumor cell killing. The platform further opens opportunities for personalized immunotherapies through the rapid development of binders against patient-specific neoantigens.

Second, I will discuss innovations in T cell manufacturing, focusing on a novel biocompatible nanoparticle-based activation and expansion platform, T-Expand. By providing efficient T cell stimulation while avoiding limitations associated with conventional bead-based systems, T-Expand supports the generation of engineered T cells with enhanced proliferative capacity, cytotoxicity, and persistence. When applied during CAR-T cell production, this approach improves antitumor efficacy and enables effective tumor control at substantially reduced cell doses.

Together, these advances illustrate how the integration of computational protein design, synthetic biology, and biomaterials engineering is reshaping the development of cellular immunotherapies. By improving both target recognition and cell manufacturing, these technologies may accelerate the creation of more effective, scalable, and personalized T cell therapies for cancer.