A Scalable Platform for Cross-HLA CAR-T Targeting of Intracellular Cancer Drivers

There is no scalable platform today that can efficiently generate peptide-specific binders to intracellular cancer targets and translate them into broadly applicable cell therapies across diverse HLA types.

Technology

This technology is an integrated peptide-centric platform for the discovery and development of CAR-T therapies targeting intracellular cancer drivers presented on peptide-HLA (pMHC) complexes.

The platform combines phage display libraries specifically tailored for pMHC targets with engineered peptide-centric CAR T cells (PC-CARs) to generate high-affinity, peptide-specific binders and translate them into therapeutics. Unlike conventional libraries that often yield HLA-biased, non-specific, or non-functional candidates, these libraries are designed to preferentially recognize the target peptide, enabling efficient identification of functional binders even within a single HLA context.

These peptide-specific binders can then be incorporated into engineered PC-CAR T cells. Through targeted modifications, these CARs can be designed to recognize the same peptide across multiple HLA alleles, enabling cross-HLA targeting and expanding patient coverage while maintaining tumor specificity.

This approach provides a scalable and differentiated strategy to access intracellular oncogenic drivers that are not addressable with conventional CAR-T therapies, while enabling the generation of higher-affinity, more selective peptide-specific binders that improve overall therapeutic performance.

Background

Approximately 84% of cancer drivers are intracellular, yet the majority of approved CAR-T therapies target surface antigens such as CD19 and BCMA, limiting target scope and contributing to on-target toxicity in healthy tissues. Peptide-HLA complexes provide a mechanism to access intracellular targets; however, HLA polymorphism fragments patient populations and reduces the commercial viability of peptide-based therapies.

Existing approaches targeting peptide-HLA complexes, including TCRs and TCR-mimic antibodies, are typically restricted to a single HLA allele, which often fail to recognize self-derived cancer peptides or generate sufficient anti-tumor activity. In addition, conventional discovery platforms frequently generate binders that preferentially recognize HLA rather than the peptide, resulting in low functional yield.

This platform addresses these limitations by enabling efficient generation of peptide-specific binders and their subsequent translation into therapeutics with the potential for broader HLA coverage.

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Category

Life Sciences/Therapeutics/Oncology
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Development Stage

NYU has generated peptide-specific binders using the discovery platform, with strong on-target binding observed in validation assays.

NYU is seeking partners interested in developing next-generation CAR-T therapies targeting intracellular oncogenic drivers using this platform.

Applications

- **Oncology:** Targeting intracellular oncogenic drivers such as KRAS, p53, MYC, β-catenin, PRAME, MAGE family proteins, and non-canonical tumor-associated peptides.
- **Broad tumor applicability:** Applicable across multiple solid and hematologic malignancies, including lung, breast, pancreatic, ovarian, colorectal, melanoma, and head & neck cancers.
- **Pan-cancer peptide targeting:** Identification and targeting of shared and non-canonical tumor antigens across multiple cancer types.
- **Rare HLA populations:** Expanding therapeutic access to patients with underrepresented HLA alleles.

Advantages

- **End-to-end platform:** Integrated system linking binder discovery to CAR-T development.
- **Expanded patient coverage:** Cross-HLA recognition enables one therapy across multiple HLA-defined populations.
- **Access to intracellular targets:** Enables targeting of major oncogenic drivers not accessible with conventional CAR-T.
- **Improved specificity and affinity:** Preferential targeting of peptide-HLA complexes reduces off-target effects and enhances binding quality.
- **Scalable discovery engine:** Enables rapid generation and optimization of new therapeutic candidates.

Intellectual Property

NYU has filed U.S. provisional patent applications covering the peptide-centric CAR T cell compositions, cross-HLA engineering strategies, structure-informed scFv libraries, screening methods, and therapeutic applications.

Importantly, NYU has developed intellectual property across the full workflow, including target discovery, pMHC-focused library design, binder screening, and CAR engineering, enabling a fully integrated platform from discovery to therapeutic development.