Strike Pharma
www.strikepharma.com

ADAC technology targeting CD40—the next step in personalized immunotherapy

Strike Pharma has developed new affinity-based linkers for optimized delivery of tumor-specific immunogenic peptides to immune cells, creating more efficacious personalized immunotherapies with fewer side effects.

Immunotherapy encompasses many different modalities, each with their particular advantages and drawbacks. Cell-based therapies, for example, can be highly effective, but are also expensive and require time-consuming and labor-intensive ex vivo procedures for their creation, especially when they are personalized to the patient's specific tumor. Antibody and peptide therapies, by contrast, often lack sufficient efficacy.

Strike Pharma is building and improving on antibody/peptide approaches, retaining their cost-effectiveness and relative ease of production while increasing their efficacy to enable the use of lower therapeutic doses, with consequently reduced side effects. At the heart of Strike's approach is the company's proprietary adaptable drug-affinity conjugate (ADAC) technology, a platform that enables immunogenic tumor-derived peptides to be attached to agonistic cluster of differentiation 40 (CD40) antibodies so that they are delivered to antigen-presenting cells (APCs), internalized, and then presented to T cells to stimulate an anti-tumor response. With ADAC, Strike is ushering in the era of precision immunotherapy (Fig. 1).

The ADAC platform uses genomic data from tumors to identify cancer-specific neoantigenic peptides, which are then synthesized with Strike's proprietary pTag linker added at one end. The pTag contains a sequence that creates an affinity interaction with the agonistic CD40 antibody, creating a cargo-loaded antibody that binds to CD40 molecules on the surface of APCs.

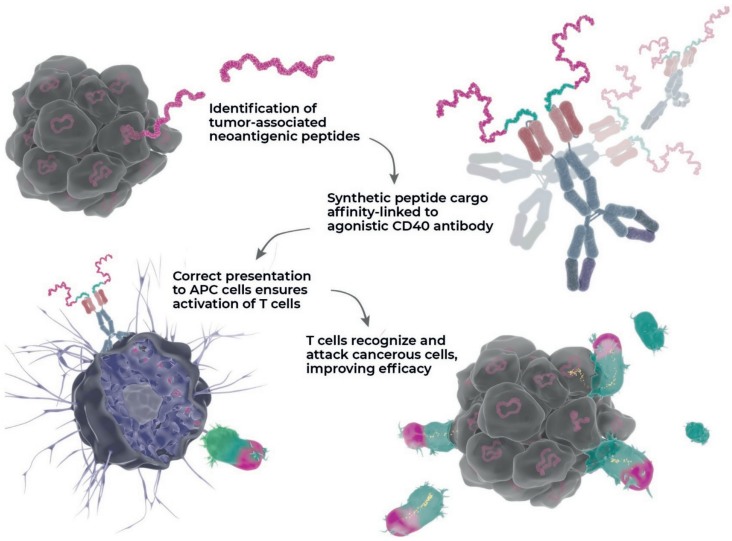

Fig. 1 | How ADAC works. 1. Tumor-associated neoantigenic peptides are identified through genomic analysis. **2.** These peptides are then synthesized, and affinity linked to agonistic cluster of differentiation 40 (CD40) antibody. **3.** The CD40 antibody binds to an APC (antigen-presenting cell) which the internalizes and presents the neoantigenic peptide. **4.** T lymphocytes recognize these presented peptides, initiating an immune response to destroy the tumor.

Multifunctional approach

Strike's CD40 antibody conjugates are truly multimodal drugs. In addition to activation of APCs through the agonist function of the CD40 antibody, APCs internalize the antibody–protein complex and present the affinity-attached immunogenic peptide to T lymphocytes, activating them and initiating an immune response to the tumor bearing the same peptide. This not only leads to targeted destruction of the tumor by the immune system, but also generates a functional immune-surveillance system to detect and destroy metastases and provide a long-lasting immune response.

Unlike cell-based approaches that involve expensive ex vivo procedures to create the therapeutic, Strike's affinity conjugation of peptides to antibodies in the ADAC platform would be performed by mixing at the hospital pharmacy, meaning that expansion of tumor-specific T cells takes place inside the body of the patient rather than ex vivo. The elegant design of ADAC generates increased bioavailability, leading to better exposure of the patient to the cargo and proper T cell expansion. The combination of the potent immune response generated by the tumor-specific cargo, and the APC-activating effects of the CD40 antibody, offers scope for reduced therapeutic doses and fewer side effects.

ADAC is a true platform technology because both the pTag linker and the CD40 antibodies are entirely agnostic with respect to their cargo: any immunogenic peptide derived from a genomic analysis of a patient's tumor can be delivered to APCs. Crucially, because the pre-selected CD40 antibodies and the pTag are already well characterized, with the only different element being the peptide cargo, potential manufacturing and regulatory obstacles are greatly reduced across drug development programs. Specifically, the synthetic-production route of the variable part of the drug opens up a regulatory opportunity that should be attractive for drug developers.

Targeting a range of cancers

Although the ADAC platform is ideal for creating individualized therapies based on the specific genomic changes and immunogenic peptides present in a given patient's tumor, Strike's most advanced asset is an off-the-shelf product designed to be applicable to a wide range of cancers—and to demonstrate the power of the ADAC technology.

Strike has selected antigens generated by mutations in *KRAS*—one of the most frequently mutated oncogenes in human cancers and present in up to 90% of pancreatic cancers, 40% of colon cancers and 20% of lung cancers (especially non-small-cell lung cancers)—as the first peptides to conjugate to CD40 antibodies and to bring through the development pipeline. As the diagnostics are already in place and in use for *KRAS* mutational status, Strike has a great opportunity for fast product uptake. The company has generated efficacy data on the platform strategy and is currently generating preclinical in vitro and in vivo data on the efficacy and safety of K-RAS–antibody conjugates, while simultaneously establishing good manufacturing practice (GMP) processes for large-scale production of the therapeutic. The company aims to submit an investigational new drug (IND) during the second half of 2024.

CONTACT
Mårten Winge, CEO
Strike Pharma
Uppsala, Sweden
Tel: +46 70 657 59 27
Email: marten.winge@strikepharma.com