Integrin α4β1-Specific DNA Aptamer Conjugates

A novel DNA aptamer-polymer conjugate designed to selectively bind integrin α4β1 (VLA-4), offering potential treatments for T-cell based autoimmune disorders and T-cell malignancies.

What is the Problem?

T cells are one of the primary cell types responsible for autoimmune inflammation in autoimmune diseases such as multiple sclerosis (MS). These T cells migrate to inflammation sites partly due to their interaction with VLA-4. Antibodies against VLA-4 are one approved therapy for MS but are an expensive treatment option.

Additionally, T-cell malignancies such as leukemia and lymphoma are challenging to treat due to the similarities between healthy and malignant T cells. Current chemotherapy treatments are nonspecific, often leading to relapsed or refractory disease. There is a critical need for targeted therapies that can effectively distinguish and treat malignant T cells without harming healthy ones.

What is the Solution?

This technology introduces a DNA aptamer, HR7A1, which binds with high affinity to integrin α4β1 (VLA-4), a marker linked to inflammation in MS and chemoresistance in leukemia patients. DNA aptamers are short, single-stranded DNA molecules that can bind to specific targets with high affinity and specificity. The technology can be used to block the binding of activated T cells to activated endothelium as a potential treatment for T-cell based auto-immune disorders such as MS. In addition, this aptamer technology has been truncated to a minimal binding motif, enhancing its specificity for T-lineage cancer cells over healthy immune cells. The HR7A1 aptamer can also potentially target and treat T-cell malignancies by binding to integrin α4β1, a marker associated with chemoresistance and relapse.

Additionally, these aptamers may be chemically modified and conjugated to various molecules to enhance their stability, reduce degradation, and improve their pharmacokinetics in the body. The innovation includes developing an aptamer-polymer conjugate to address challenges such as serum stability and short circulation half-life, making it a promising candidate for targeted autoimmune and cancer therapies. This approach offers a promising alternative to traditional antibody-based therapies, potentially lowering costs and increasing accessibility.

What is the Competitive Advantage?

Technology ID

BDP 8881

Category

Selection of Available Technologies

Therapeutics/Other

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High Specificity: The HR7A1 aptamer selectively binds to integrin α4β1, ensuring targeted treatment of T-cell based autoimmune disorders and T-cell malignancies.

Cost-Effective Production: Aptamers can be synthesized more cheaply and easily than antibodies, making the technology more accessible.

Enhanced Stability: The aptamer-polymer conjugate improves serum stability and circulation time, addressing issues of degradation and rapid clearance.

Reduced Side Effects: By targeting only malignant T cells, this technology minimizes damage to healthy cells, reducing the side effects commonly associated with chemotherapy.

Potential for Combination Therapy: The aptamer's binding site overlaps with fibronectin and VCAM-1, which may enhance the effectiveness of existing chemotherapy treatments.

References

1. Cardle, I. I., Raman, J., Nguyen, D. C., Wang, T., Wu, A. Y., Sellers, D. L., Pichon, T. J., Cheng, E. L., Kacherovsky, N., Salipante, S. J., Jensen, M. C., Pun, S. H.(2025) , https://pubmed.ncbi.nlm.nih.gov/39788927/, https://pubs.acs.org/journal/aamick, 17, 4543-4561