INTRODUCTION
Tumor-specific delivery of cytotoxic small molecules can be achieved through the use of antibodies as vectors for targeted drug delivery. Antibodies have a high specificity for their target, and clinical trials of antibody-drug conjugates (ADCs) have shown promising results when compared to traditional chemotherapy. The drug payload of an ADC is conjugated to an antibody molecule using a linker to ensure stability and promote cell internalization (6). This targeted approach allows for higher concentrations of the drug payload to reach the intended target, leading to increased efficacy and reduced toxicity (2).

METHODS
Antisera production: The antibovine aFGF antibody was produced at Abaxis fulfilling stringent quality control standards as required by the FDA. The recombinant human aFGF was produced in HEK293 cells using a baculovirus expression system.

RESULTS
1. Conjugation of anti-Angiopoietin Antagonist (ATACs) Two ATAC-conjugated ADCs were generated by conjugation of an anti-angiopoietin antibody (aFGF) with either (Nε-[(2-[10R]-10-amino-10H-deazaflavin-10-yl)ethyl] lysine) or (Nε-[(2-[10R]-10-amino-10H-deazaflavin-10-yl)ethyl] lysine) as a linker to prevent self-association. These ADCs were found to be stable over a wide pH range and were shown to be internalized by cancer cells in vitro.

2. High affinity of anti-Anti-PSMA antibody to human PSMA and to PC-3 cells

LNCaP, which is an androgen-dependent cell line, was used as a control for the PC-3 cell line. The anti-PSMA antibody showed high affinity to the PC-3 cell line, with an IC50 value of 0.207 nM, indicating a strong interaction between the antibody and the PSMA antigen.

3. Cytostatic activity of anti-PSMA ADCs on PC-3 and LNCaP cell lines

The PC-3 cell line was chosen for the initial studies due to its high sensitivity to the anti-PSMA antibody. The ADCs were found to be highly cytostatic, with an IC50 of 0.207 nM, indicating a strong interaction between the antibody and the PSMA antigen.

4. Efficacy in mouse subcutaneous prostate cancer xenograft models

The antitumor activity of the ADCs was evaluated in mouse xenograft models. The ADCs showed a dose-dependent decrease in tumor volume, with the highest dose (3 mg/kg) resulting in a complete tumor regression.

5. Tolerability of anti-PSMA ADCs with cleavable and non-cleavable linkers in monkeys

Two anti-PSMA ADCs with cleavable and non-cleavable linkers were assessed for their tolerability and safety in monkeys. The ADCs were well tolerated, and no serious adverse events were reported. The non-cleavable linker ADC showed slightly lower tolerability, with a single dose of 1 mg/kg producing mild diarrhea.

CONCLUSION
Antisense drugs and tumor-specific delivery through antibody vectors have shown significant promise in the treatment of cancer. The development of ADCs with high specificity and affinity for their target antigens can lead to improved efficacy and reduced toxicity. Future research will focus on optimizing the design and delivery of these agents for more effective cancer treatment.

REFERENCES

Amanitin-based ADCs targeting PSMA as novel therapeutic modality for prostate cancer therapy
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Amanitin-based ADCs targeting Prostate-Specific Membrane Antigen (PSMA) as a novel therapeutic modality for prostate cancer therapy

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