ENHANCING ANTIBODY THERAPEUTICS VIA GLYCAN ENGINEERING AND INTRACELLULAR DYNAMICS CONTROL

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The development of antibody therapeutics has revolutionized cancer treatment, offering high target specificity and potent immune-inducing activities such as antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Enhancing these activities remains a significant focus in both academic and industrial research.
In our recent study, we aimed to control antibody dynamics and enhance immune-inducing activity by utilizing glycan-lectin interactions. Specifically, we introduced galactose-containing glycans to anti-HER2 antibodies—therapeutic agents for breast cancer—and successfully suppressed antibody internalization through binding to galectin-3. This led to a significant enhancement in CDC activity [1]. Further live-cell imaging analysis revealed that interactions between glycan-modified antibodies and the galectin lattice on the cell surface are crucial in inhibiting internalization [2].
In addition, we explored nuclear medicine therapy using the alpha-emitting isotope astatine (^{211}At), which has shown promise due to its high cancer-killing efficacy and limited side effects. We developed radioimmunotherapy complexes (RICs) by labeling anti-glypican-1 antibodies with ^{211}At for targeted therapy in pancreatic cancer models.[3] By incorporating intracellular enzyme cleavage sites and nuclear translocation signal peptides into the antibody linker region, we significantly enhanced the cytotoxic effect of ^{211}At.[4]
These findings demonstrate that controlling antibody dynamics through glycan engineering and advanced radioisotope conjugation strategies is a promising approach for improving the therapeutic efficacy of antibody-based cancer treatments. Our ongoing research strives to translate these innovations into clinical applications, with the ultimate goal of developing next-generation antibody therapeutics.

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