OPEN ACCESS Freely available online

ISSN: 2167-1052
Advances in Pharmacoepidemiology and Drug Safety

Commentary

Transforming Disease Targeting with Bio-Orthogonal Chemistry and Glycan Engineering

Hanae Fujimoto*

Department of Public Health, Osaka Central Medical University, Osaka, Japan

DESCRIPTION

Metabolic glycan labelling combined with bio-orthogonal targeting represents a powerful and emerging strategy in the field of targeted drug delivery. This technique capitalizes on the natural biosynthetic pathways of glycans in mammalian cells, modifying them with chemical handles that are inert to biological systems yet reactive to complementary chemical probes. The result is a highly selective, non-invasive method for cell surface engineering that holds significant promise for precision therapeutics, especially in cancer and inflammatory diseases.

Glycans are essential components of the cell surface and play critical roles in cell-cell interactions, immune recognition and pathogen binding. Importantly, aberrant glycosylation patterns are hallmarks of many disease states, particularly cancer, where overexpressed or altered glycan structures are frequently observed. Metabolic glycan labelling exploits this principle by feeding cells synthetic monosaccharide analogues such as N-azidoacetylmannosamine (ManNAz), which are metabolically incorporated into glycoconjugates. The azide functionality introduced into the glycans serves as a bio-orthogonal handle for subsequent selective reaction with probes carrying reactive groups like alkynes or strained cyclooctynes *via* click chemistry.

What sets this approach apart is its dual advantage of specificity and modularity. Because the modified sugars are incorporated into glycan structures only in metabolically active cells, particularly those with high glycosylation turnover, the technique inherently targets rapidly dividing or diseased cells more than normal tissues. The bio-orthogonal reaction then allows for conjugation of imaging agents, drugs, or nanoparticles without interfering with endogenous biomolecules, enabling high-resolution tracking and targeted payload delivery.

Recent studies have demonstrated the feasibility of this approach *in vivo*. For example, azide-labelled tumor cells have been selectively targeted with Dibenzocyclooctyne (DBCO)-conjugated nanoparticles carrying chemotherapeutic drugs, resulting in improved drug accumulation at the tumor site and enhanced antitumor efficacy with reduced systemic toxicity. Similar strategies have been applied to label and target inflammatory cells in models of rheumatoid arthritis and colitis, suggesting broad applicability beyond oncology.

One of the most compelling aspects of metabolic glycan labelling is its adaptability. The metabolic precursors can be fine-tuned to target specific glycan biosynthetic pathways and the bio-orthogonal chemistry toolbox continues to expand with faster and more selective reactions. This opens the door for real-time, *in situ* modification of living tissues with minimal off-target effects. Moreover, coupling this approach with stimuli-responsive drug carriers or theranostic systems could enable dynamic control over drug release and monitoring of therapeutic outcomes.

Despite its potential, several challenges remain before clinical translation. First, the pharmacokinetics and safety of unnatural monosaccharide analogues must be thoroughly assessed, particularly with repeated or long-term administration. Second, the efficiency of metabolic incorporation can vary among different cell types and disease models, potentially limiting uniform targeting. Third, bio-orthogonal reactions, while fast and selective *in vitro*, may face diffusion and accessibility limitations in complex tissue environments. Addressing these concerns will require optimization of sugar analogues, reaction conditions and delivery vehicles.

Additionally, regulatory and manufacturing considerations must be taken into account. The integration of metabolic glycan labelling into a clinical drug delivery platform involves multi-component systems synthetic sugars, targeting chemistries and payload carriers all of which must comply with rigorous safety and reproducibility standards. Advances in nanoparticle formulation, bioconjugation techniques and quality control analytics will play a significant role in bridging the gap from bench to bedside.

Correspondence to: Hanae Fujimoto, Department of Public Health, Osaka Central Medical University, Osaka, Japan, E-mail: h.fujimoto@ocmu.jp

Received: 19-Feb-2025, Manuscript No. PDS-25-28726; **Editor assigned:** 21-Feb-2025, PreQC No. PDS-25-28726 (PQ); **Reviewed:** 07-Mar-2025, QC No. PDS-25-28726; **Revised:** 14-Mar-2025, Manuscript No. PDS-25-28726 (R); **Published:** 21-Mar-2025, DOI: 10.35250/2167-1052.25.14.386

Citation: Fujimoto H (2025). Transforming Disease Targeting with Bio-Orthogonal Chemistry and Glycan Engineering. Adv Pharmacoepidemiol Drug Saf. 14:386.

Nevertheless, the potential benefits of this technology are too significant to ignore. Targeted drug delivery remains one of the most desired goals in medicine, with the promise of enhancing therapeutic efficacy while minimizing adverse effects. Metabolic glycan labelling provides a unique and versatile entry point into the disease microenvironment, enabling selective intervention with unprecedented precision.

In conclusion, metabolic glycan labelling with bio-orthogonal targeting is more than a sophisticated chemical trick; it represents a change of opinion in how we approach disease targeting and drug delivery. While challenges in scalability, safety and standardization exist, the foundational science is sound and early results are encouraging. Continued interdisciplinary collaboration between chemists, biologists and clinicians will be essential to control the full potential of this innovative strategy and to unlock its translational value in future therapeutic applications.