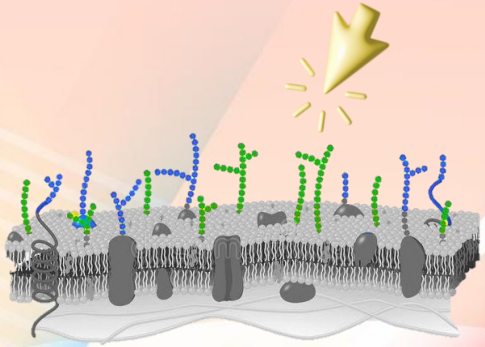

Sweet Encounters: Studying Nanoparticle-Glycan Interactions by Metabolic Labeling and Click Chemistry

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CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

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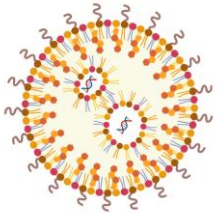
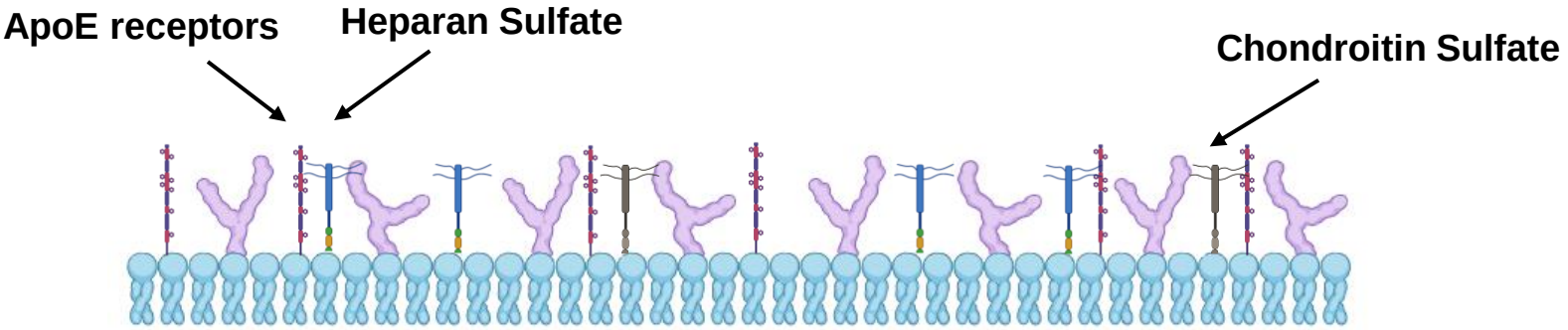


Nanoparticles

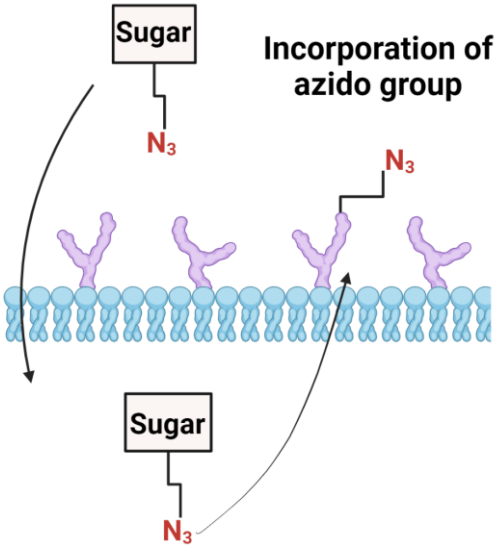


Glycocalyx: the first point of contact with nanoparticles

Akinc, A. *et al.* The Onpattro story and the clinical translation of nanomedicines containing nucleic acid-based drugs. *Nat. Nanotechnol.* **14**, 1084–1087 (2019).

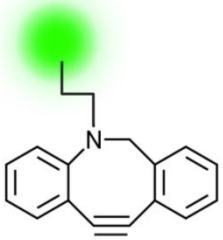
Principle

Metabolic Labelling

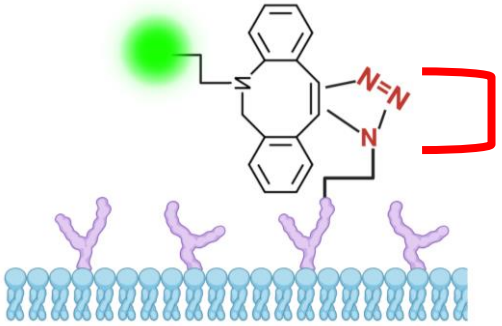


Metabolism of azido sugar inside cell

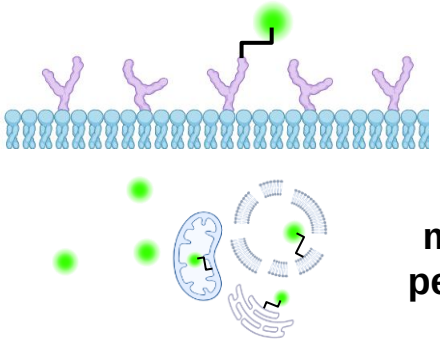
Click Chemistry



DBCO

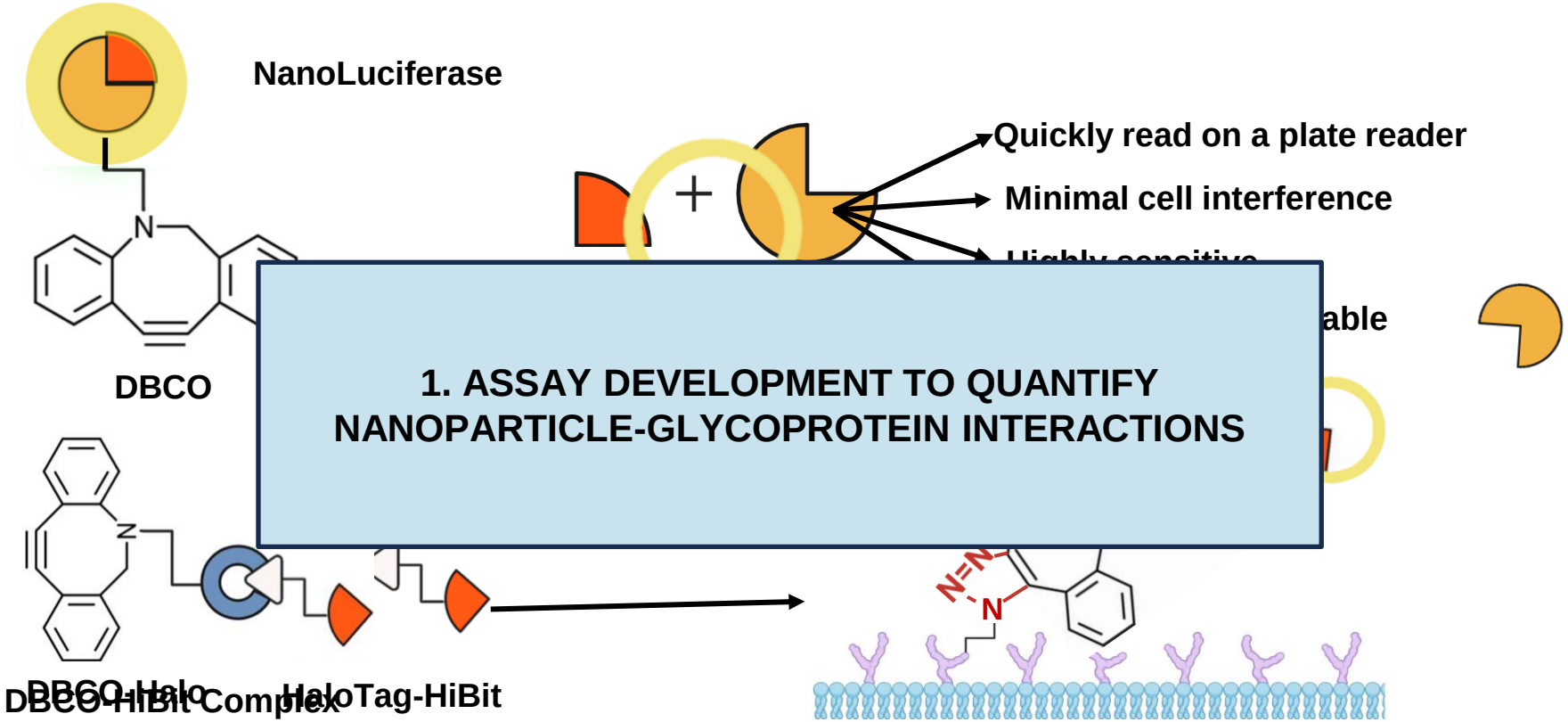


Tedious and lengthy

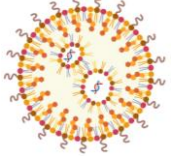


Cell membrane permeability

Lam YY, et. al. Metabolic glycan labelling with bio-orthogonal targeting and its potential in drug delivery. J Control Release. 2025 Feb 10;378:880-898.



1. ASSAY DEVELOPMENT TO QUANTIFY NANOPARTICLE-GLYCOPROTEIN INTERACTIONS

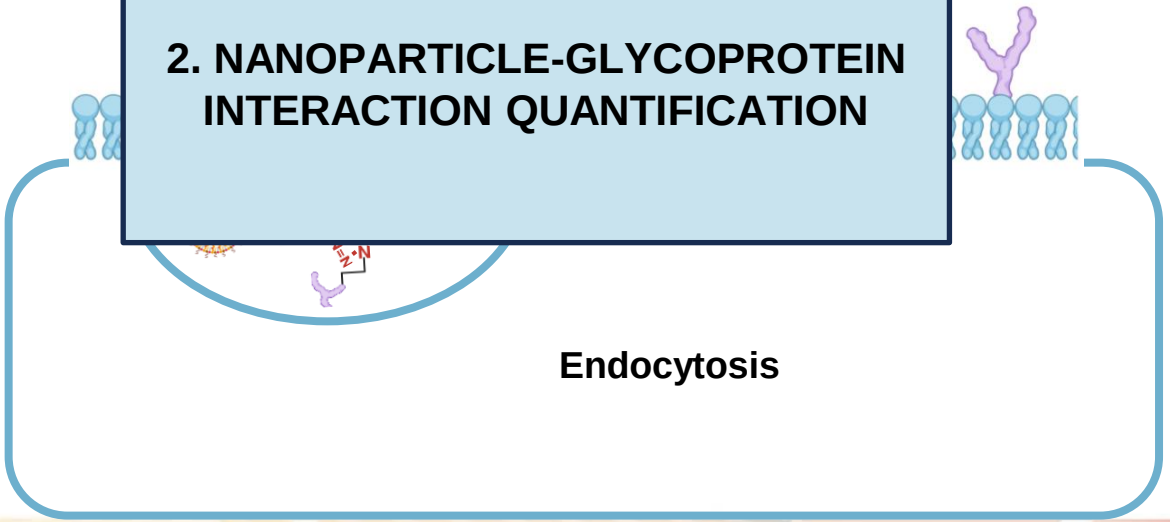


FDA approved Nanoparticles

Luminescence signal

Uptake by glycoproteins

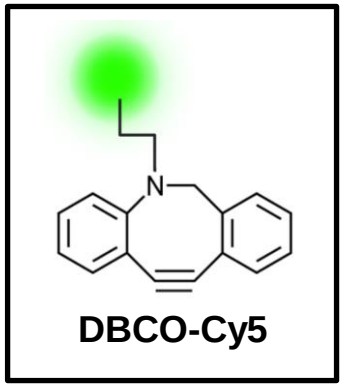
2. NANOPARTICLE-GLYCOPROTEIN INTERACTION QUANTIFICATION

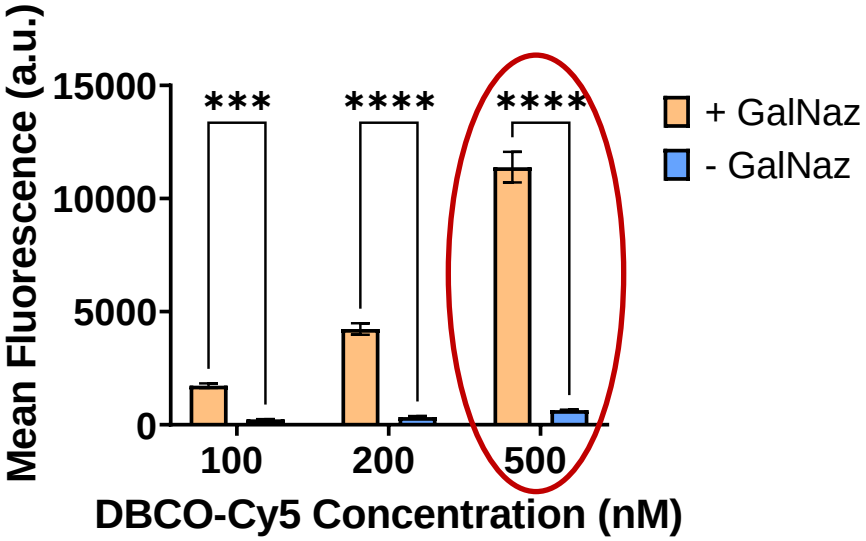


Endocytosis

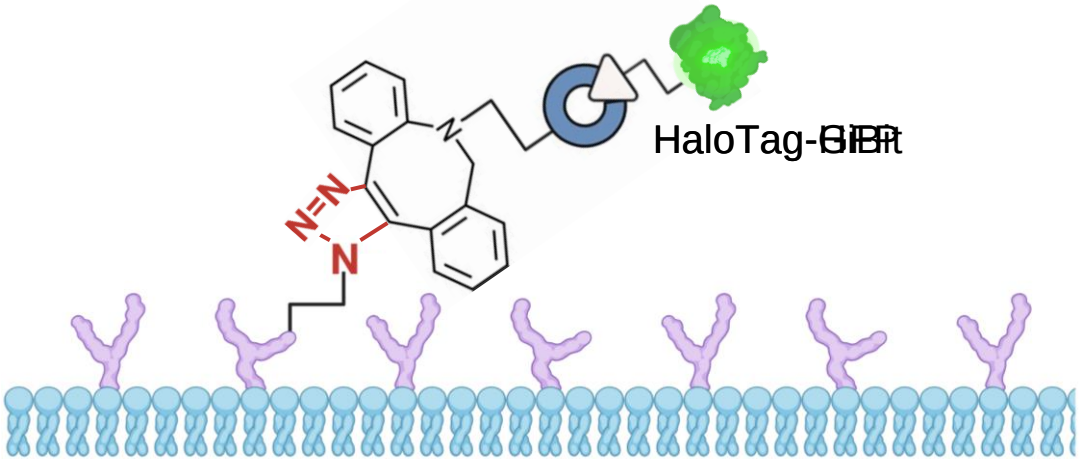
Results

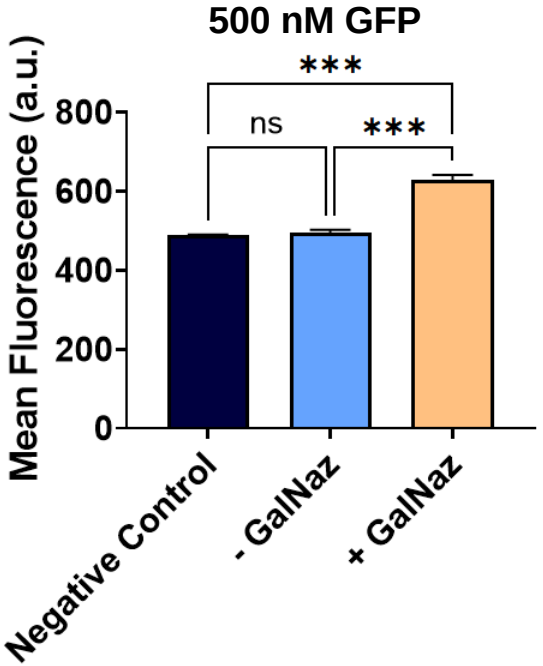
1. Metabolic labelling using traditional linkers showed high efficiency



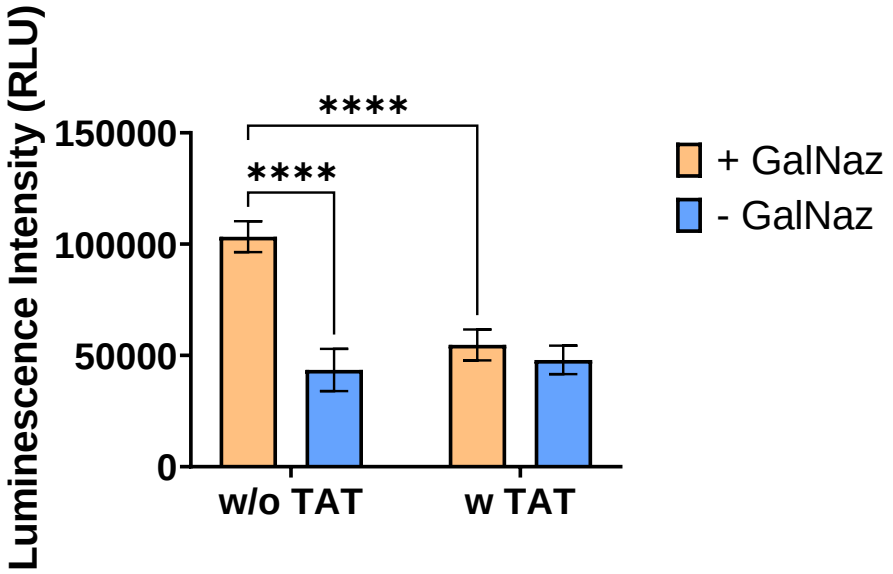


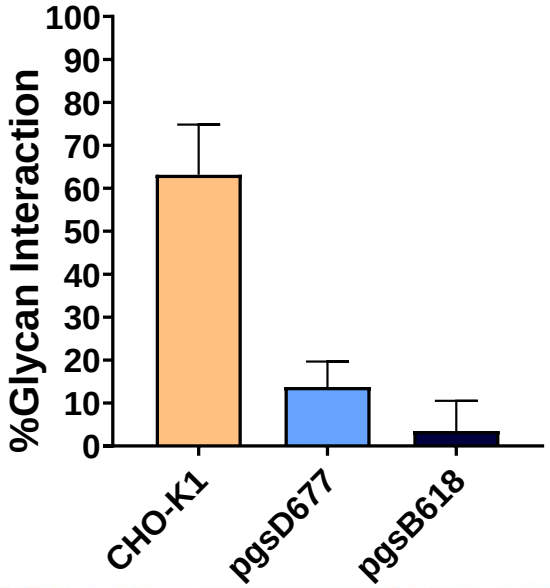
2. Proof of Concept DBCO-GFP assay showed promising results





3. DBCO-HiBit assay shows differential signal/noise ratio and signal decrease with glycan mediated endocytosis

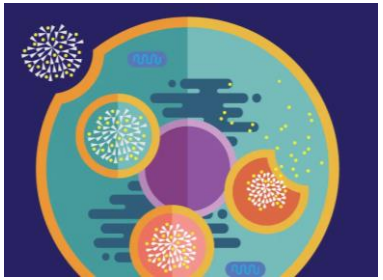




Future Prospects

- Quantify glycoprotein interactions by developing LNPs with varied lipid molar ratios and physicochemical properties.
- Quantify glycoprotein interactions by developing pegylated polymeric nanoparticles with varied physicochemical properties.

Acknowledgments



Intracellular Drug Delivery

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