

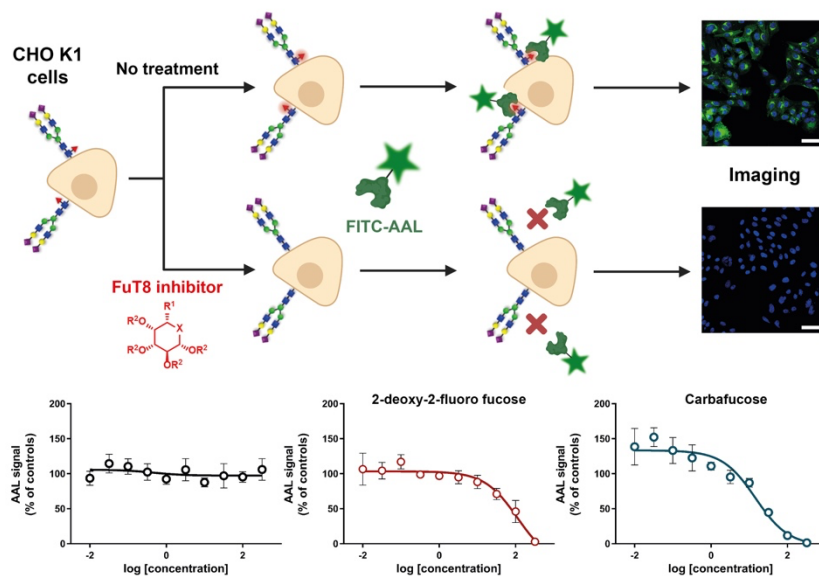
A new non-incorporable metabolic inhibitor enables production of a fucosylated therapeutic antibodies

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Glycosylation is a post-translational modification involved in many biological processes. This functional diversity is mirrored in a great structural diversity. Among the various monosaccharides is L-fucose, commonly found in terminal positions within glycans. Fucose residues mediate a range of biological effects, from regulation of leukocytes during inflammation to binding of IgG antibodies to Fc gamma receptors. Accordingly, there is great interest in developing tools to modulate cellular fucosylation. To date, the most successful approach pursued to block fucosylation has been the development of metabolic inhibitors: synthetic fucose mimetics able to hijack the biosynthetic pathway and to block the enzymes responsible for transfer of fucose onto glycans.¹ Existing metabolic inhibitors of fucosylation are limited in their application due to undesirable low-level incorporation into glycans which can raise concerns for industrial or therapeutic applications.² To address these concerns, we designed, synthesized, and used carba-fucose as an efficient new metabolic fucosylation inhibitor that is assimilated into the *de novo* biosynthetic pathway and potently blocks cell fucosylation. We further demonstrated that carba-fucose was not transferred onto resulting glycans and could, therefore, be used to produce afucosylated antibodies to enhance their efficacy for therapeutic applications. We expect that, more generally, carba-fucose will find common use as a research tool to block cellular fucosylation and to enable fundamental studies into the physiological roles of fucosylation.



Lectin-based fucosylation assay in CHO K1 cells

Bibliographic references:

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- (2) Y. Kizuka, *Biochim. Biophys. Acta BBA - Gen. Subj.* 2022, 1866 (12), 130243