GLYCOBIOLOGY

Selective cell-surface N-glycan editing

A two-step chemoenzymatic method for N-glycan subtype-selective editing.

High heterogeneity of N-glycans on cell surface glycoproteins makes understanding their precise functional role very challenging. A variety of chemical biology approaches, such as metabolic glycan labeling, selective oxidation and glycosyltransferase-catalyzed modification, have been developed and utilized for cell surface glycan labeling and imaging. However, differentiating between N- and O-glycans and their subtypes, or selectively changing the heterogeneous nature of surface N-glycans, is not straightforward.

Wei Huang and colleagues from the Chinese Academy of Sciences have developed a method for selectively deleting a subclass of N-glycans and converting these sites to well-defined N-glycan structures using a series of bacterial

endoglycosidases. “The key feature of our method is the controllable editing on certain N-glycan subtypes such as core-fucosylated or non-core-fucosylated, or global glyco-editing on a Lec4 CHO cell line,” explains Huang.

As an example, the researchers expressed a G-protein-coupled receptor, opioid receptor- $\delta 1$ (OPRD1), in Lec4 CHO cells. They then used a two-step glycan-editing approach to edit the heterogeneous cell surface glycans to well-defined glycans to reveal their roles in receptor signaling, dimerization and internalization. “It is kind of surprising that the glycan of OPRD1 receptor does not affect the ligand-induced signaling, though the glycan is involved in receptor stabilization and internalization,” explains Huang. Further investigation of receptor activation, desensitization and

restoration would be required to better understand this.

To expand the method into a comprehensive cell surface glyco-editing toolkit, the authors think more efficient and diverse enzymes are needed, and this would require enzyme engineering or discovery. They are looking forward to applying the method to understanding other membrane receptors and further developing strategies to interfere with receptor glycosylation.

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Published online: 2 July 2020

<https://doi.org/10.1038/s41592-020-0896-7>

Research paper

Tang, F. et al. Selective N-glycan editing on living cell surfaces to probe glycoconjugate function. *Nat. Chem. Biol.* <https://doi.org/10.1038/s41589-020-0551-8> (2020).

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