

## A genetic entry point to harness the untapped potential in glycobiology

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Breakthroughs in O-glycobiology have gone hand in hand with the development of new technologies, such as advancements in mass spectrometry and the facilitation of genetic engineering in mammalian cell lines. High-throughput glycoproteomics has enabled us to draw a comprehensive map of O-glycosylation and mining this information has supported the discovery of functions related to site-specific O-glycans, such as protection from proteolytic cleavage and modulation of receptor functions. Yet, there is still much to discover.

Among the important next challenges will be to define the contextual functions of glycans in cellular metabolism, host-microbiome interactions, and different stages of cellular differentiation. We have used a genetic entry point and targeted specific glycogenes to generate a library of cell and tissue models that selectively differ in their capacity to produce specific glycan structures.

The engineered libraries can be used to define how glycan-binding proteins recognize glycans in the context of the cellular membrane and how specific glycans impact tissue formation and homeostasis. Furthermore, the engineered cells are instrumental in developing new glycan-based treatments, including potent immunotherapies targeting cancer-associated O-glycans.