Highlights 2018

Copenhagen Center for Glycomics continues to focus on diseases caused by defects in the biosynthesis and structure of complex carbohydrates. We use a genetic approach to dissect and discover biological roles of glycosylation. In the second phase of our DNRF program we are going global to gain comprehensive understanding and control of glycosylation pathways. We are developing new tools and technology platforms that will break through barriers for the field, enabling wider consideration of the opportunities for discovery and applications. We reported the first example of this strategy in 2018 with introduction of the Cell-Based Glycan Display for glycosaminoglycans – The GAGOme (Figure Chen *et al.* **Nat Methods**). Cell-Based Glycan Arrays are self-renewable and sustainable resources that can be readily used for dissection and discovery of functions of glycans. They represent a cornerstone in our vision of transforming glycomics from a closed expert field to a true Omics approachable by all cell biologist. The Cell-Based Arrays provide direct information of the genetic and biosynthetic basis for the queried biological phenomenon with simple predictions of the actual glycan structures involved.

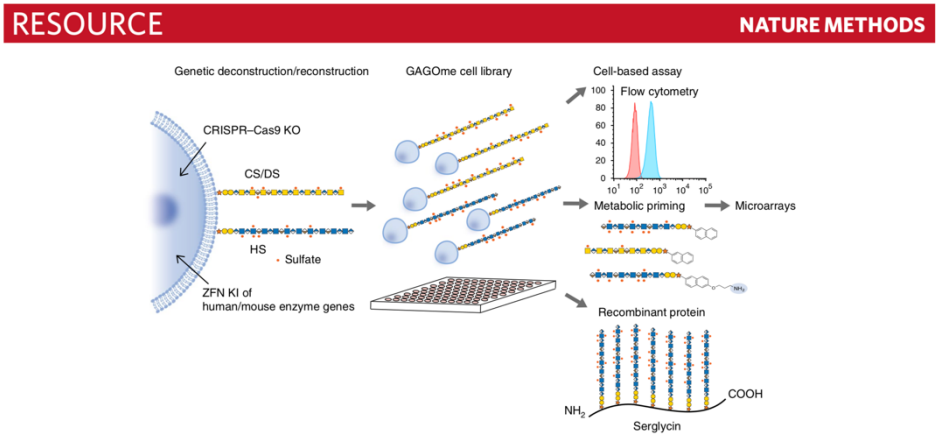

Fig. 1 | Graphic depiction of the GAGOme approach. Genetic engineering by targeted KO with CRISPR–Cas9 or targeted KI with a zinc-finger nuclease (ZFN) generates a library of isogenic cells displaying different repertoires of GAG structures. The GAGOme cell library can be used to dissect the specificities of GAG-binding proteins by flow cytometry, for the production of recombinant proteoglycans with distinct GAG chains, and for metabolic priming with xylosides ($XylNapNH_2$) to generate libraries of distinct GAG chains suitable for microarrays.

Genetic dissection of glycosylation pathways continue to reveal groundbreaking discoveries, and this year we showed that site-specific O-glycosylation modulates the functions of lipoprotein receptors (LDLR/VLDLR) (Wang *et al.* **JBC**) in a tightly regulatable process (Hintzen *et al.* **JBC**). We used our glycogene engineering strategy to produce homogeneous glycoforms of therapeutic glycoproteins that enables native top-down mass spectrometry characterization and quality control (Caval *et al.* **Nat Commun**), and to engineer new allergy vaccine designs with glycomodules (Mathiesen *et al.* **J Allergy Clin Immunol**). We reported a series of studies providing a global views of glycosylation pathways and the genetic and biosynthetic regulation (Joshi *et al.* **Cell**, Narimatsu *et al.* **Glycobiology**), which forms the foundation for our ambition for developing *in silico* glycomics strategies.

We made other major scientific breakthroughs in 2018, which are being published early 2019. We are poised for the quantum leap in the field of glycomics as predicted, and our program continues to expand with exciting developments. The co-PI was awarded a Consolidator ERC grant, and the PI the Society for Glycobiology President's Innovator Award in 2018. We continue translational activities and our spin-out, GlycoDisplay ApS, has brought direct involvement of industry. In short, the program continues to thrive and develop.