Highlights 2019

Copenhagen Center for Glycomics focuses 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 and identify opportunities for novel biomedical applications. At the end of our DNRF era, we are well underway with transforming the program for a new phase as pioneer and leader in *in silico* and systems biology approaches to glycomics. We developed the first sustainable cell-based glycan arrays with expansion to all types of glycans for display and interrogation of functions of glycans (Narimatsu *et al.* **Molec Cell**). We expanded the CHO cell library for recombinant production of glycoprotein therapeutics with well-defined glycans, which has led to a new design concept for lysosomal replacement enzymes that provides improved biodistribution and therapeutic efficacy (Tian *et al.* **Nat Commun**). We used our SimpleCell O-glycoproteomics strategy to discover O-glycans on the natriuretic peptide ANP, which provides novel opportunities for design of therapeutic intervention for heart failure (Hansen *et al.* **JBC, Editors pick**).

EDITORS' PICK HIGHLIGHT: *Glycans modulate natriuretic peptides*

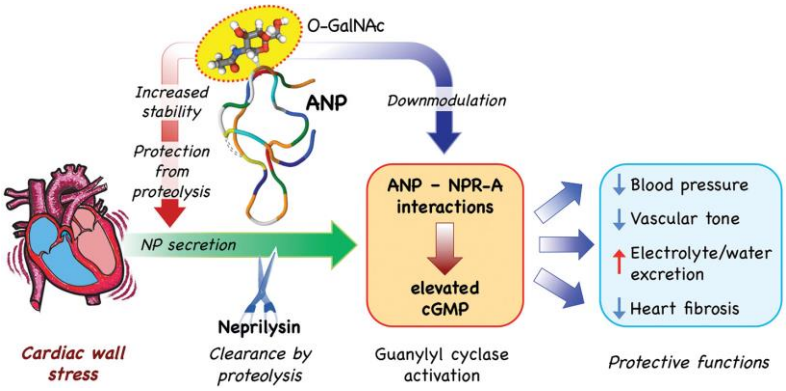

Figure 1. Proposed mechanism for *O*-GalNAc–mediated modulation of ANP function. In response to increased cardiac wall stress, the heart secretes ANP into the circulation. ANP elevates cGMP levels by activating guanylyl cyclase activity of NPR-A, resulting in protective functions, such as lowering blood pressure, affecting diuretic and vasodilatory homeostasis, and preventing cardiac fibrosis. ANP is rapidly removed from the circulation by action of specific h il i G S hj ld d ll h h i f ANP b O l l d hi h i ANP bili b

We also continued our studies of regulation of the LDLR-related endocytic receptors by GALNT11 directed site-specific O-glycosylation, and we could validate a causative role of the GALNT11 glycosyltransferase in chronic kidney decline implied by GWAS (Tian *et al.* **PNAS**).

Our unique cancer immunotherapy program targeting aberrant O-glycopeptide epitopes continues to develop with better understanding of how our antibodies perform as CAR-Ts (He *et al.* **JCI Insight**), and our antibody 5E5 is now in an open clinical trial at UPENN/Tmunity with the first patients in treatment. Finally, we took a first step towards direct analysis of O-glycoproteins without the enrichment step currently needed, which opens the way for entirely new ways of detecting protein glycosylation heterogeneity in clinical samples (Ye *et al.* **Nat Methods**).

We continued to make other major scientific breakthroughs in 2019, which are being reported in 2020. Our focus on the next phase for CCG takes some toll on other tasks, but the team and program continues to expand with exciting developments. Our spin-out, GlycoDisplay Aps, continues to bring involvement of industry in our translational activities, but securing sufficient funding from partnerships in 2019 was challenging.