Expanding our View of the Cardiac Surfaceome: New Bioinformatic Tools and Technologies for Mapping Glycoproteins and Glycans from Small Sample Sizes

Dr Rebekah Gundry
University of Nebraska Medical Center, Omaha, Nebraska, USA.

Abstract

Cell surface glycoproteins and glycans play critical roles in a range of biological functions and disease processes, from maintaining cellular structure and adhesion to controlling how cells send and receive exogenous signals in a complex environment. Despite their critical roles in cardiac development, disease, and drug uptake, we do not yet have a detailed cell type- or chamber-resolved view of the cell surface glycoproteome or glycome of the adult human heart. Combining advanced strategies to isolate individual cardiac cell types with the recently developed CellSurfer Platform, which integrates a microscale Cell Surface Capture method for the identification of cell surface glycoproteins from small sample sizes, automated data processing workflows, and SurfaceGenie for cell-type specific marker prioritization, new views of the human heart are emerging. To date, we have identified >650 cell surface N-glycoproteins on primary human cardiac myocytes and fibroblasts, including proteins not previously described in these cell types and putative cell-type and chamber-specific markers. Additionally, a structure-based glycomics approach reveals >110 glycan structures in cardiac myocytes, which complement and inform glycoproteomic efforts. Overall, these data represent the first major step towards a cell-type, subtype, and chamber-resolved reference map of cell surface glycoproteins and glycans in the adult human heart and reveal new potential targets for immunophenotyping, in vivo imaging, drug delivery, and benchmarking cardiomyocytes derived from human pluripotent stem cells. Moreover, these data inform caveats regarding the use of explanted cardiac fibroblast models, reveal new molecular targets to study in the context of cardiac fibrosis and heart failure, and will promote studies aimed at gaining a better understanding of cross-talk among cardiac cell types in health and disease.

Biography

Dr. Gundry completed her PhD at Johns Hopkins University School of Medicine with Dr. Robert Cotter, her postdoctoral work at the NHLBI Proteomics Center at Johns Hopkins with Dr. Jennifer Van Eyk, and a visiting fellowship at ETH, Zurich with Drs. Bernd Wollscheid and Ruedi Aebersold. She was awarded an NHLBI R01 and established her independent laboratory at the Medical College of Wisconsin in 2010. In 2017 she was appointed inaugural Director of the MCW Center for Biomedical Mass Spectrometry Research. In August 2019, she was recruited to the University of Nebraska Medical Center in Omaha, NE. In addition to her role as Department Vice Chair, she is Assistant Chief of Basic and Translational Research for the Division of Cardiology and is the inaugural Director of the CardiOomics Program, which applies mass spectrometry technologies for advancing basic and translational cardiac research and clinical care. Overall, the Gundry lab develops and applies innovative mass spectrometry approaches to study cell surface proteins and glycans to answer outstanding questions in stem cell and cardiac biology and disease, and is funded by the American Heart Association, Juvenile Diabetes Research Foundation, and two NHLBI R01 awards. Rebekah received the inaugural Robert Cotter Young Investigator Award from US HUPO in 2013, Outstanding Graduate and Medical School Educator Awards in 2017 and 2018, and was recently appointed Associate Editor of the Journal of Molecular and Cellular Cardiology.