IDENTIFICATION OF ONCOGENE CONTROLLED SIALOSIDES

Benjamin A. H. Smith[a,b,†] Anja Deutzmann[c,†], Kristina Correa[d], John Pluvinage[e], Chris Dove[f], Ravindra Majeti[f], Dean Felsher[c], and Carolyn Bertozzi[a,b,d]

[a]Chemistry, Engineering, and Medicine for Human Health (ChEM-H), Stanford University, Stanford, CA, USA
[b]Department of Chemical & Systems Biology, Stanford School of Medicine, Stanford, CA, USA
[c]Division of Oncology, Stanford School of Medicine, Stanford, CA, USA
[d]Department of Chemistry, Stanford University, Stanford, CA, USA
[e]Institute for Stem Cell Biology and Regenerative Medicine, Stanford School of Medicine, Stanford, CA, USA
[f]Cancer Institute, Stanford School of Medicine, Stanford, CA, USA
[†]Equal contribution

Elevated display of the sugar sialic acid on the surface of tumor cells correlates with aggressive phenotypes. While glycans containing sialic acid ("sialosides") have long been known to promote cell adhesion and motility, they have more recently been implicated in immune evasion. Despite increasing recognition that tumor cell sialosides are important contributors to tumorigenesis, the determinants of sialoside synthesis in cancer are not well characterized.

Here, we describe a transcriptional program for sialoside synthesis in leukemia and identify oncogene controlled glycans. By performing RNA-sequencing, we establish the sialyltransferases as an important nexus for oncogene directed remodeling of the glycocalyx. Through N- and O- glycomics analyses, we discern sialosides that are displayed in an oncogene dependent fashion. We synthesized glycopolymers comprising sialosides of interest displayed on a poly(methyl vinyl ketone) backbone to assess the sufficiency of these glycans for modulating immune function. Finally, we demonstrate that oncogene controlled sialosides promote tumor engraftment and growth in a mouse model of T-acute lymphoblastic leukemia.