Inhibitors of the human neuraminidase enzymes as probes for glycobiology

The plasma membrane contains a wide array of glycans and glycolipids, most of which are capped by sialic acids (also called N-acetyl neuraminic acid, Neu5Ac). As a result, sialic acids are front-line mediators of interactions between the extracellular surface and the environment. Examples include host-pathogen interactions (e.g. influenza) and the recognition of host cells by leukocytes (white blood cells). Thus, the composition of sialosides in the membrane can influence receptor-receptor interactions critical to immunity and cellular function. Our group is investigating the influence of sialic acid on the function of adhesion and immune receptors through the development of tools that alter catabolism of membrane sialosides.

The human neuraminidase enzymes (NEU; also called sialidases) are a family of four isoenzymes (NEU1, NEU2, NEU3, and NEU4) which have wide variability in their substrate preferences as well as cellular and tissue localization. Specific functions of this enzyme family continue to be investigated, and the development of isoenzyme-selective inhibitors has provided new tools for *in vitro* and *in vivo* studies. Due to a lack of structural data on most of the isoenzymes, development of new inhibitors requires the synthesis of candidate inhibitors and screening for activity. Our group has developed a panel of selective inhibitors, many with nanomolar potency, which we are using as tools to investigate systems where NEU may play important roles. Applications of inhibitors to understanding the role of specific isoenzymes in cell migration and cell adhesion will be discussed.

Christopher W Cairo, Ph.D.

[Short bio <250 wds]

Christopher W. Cairo is a Professor of Chemistry at the University of Alberta. He obtained a BSc in Chemistry from the State University of New York (SUNY) at Albany. He went on to graduate studies at the University of Wisconsin-Madison, with Prof. Laura L. Kiessling where he worked on multivalent carbohydrate-protein interactions. Chris then moved to an NIH-funded Postdoctoral fellowship with Prof. David E. Golan at Harvard Medical School where he studied the regulation of integrins in T cell adhesion. Chris joined the faculty of the University of Alberta in 2006 as an Assistant Professor of Chemistry and was promoted to Associate Professor in 2012, and Professor in 2019. He was a principal investigator in the Alberta Glycomics Centre and is currently a Network Investigator with GlycoNet. The Cairo research group studies the function of glycoproteins and glycolipids in cardiovascular disease, cancer, and immunity. Their work takes place at the chemistry-biology interface with major projects targeting the design of inhibitors for the human neuraminidase enzymes, the recognition of carbohydrate antigens in immune response, and bioconjugate labelling strategies for glycolipids and glycoproteins.

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